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INTRODUCTION OF THE CARMAN LECTURER

By WALTER C. HILL, M.D., *Cleveland, Ohio*

MR. President, Dr. Golden, fellow members of the Radiological Society of North America and honored guests:

Each year we gather to pay tribute to the memory and inspiration of Dr. Russell D. Carman. The Carman Lecturers and those who have introduced the Carman Lecturers have often told of his energy, his keenness of observation, his intellectual honesty, common sense and trustworthy professional judgment. The dramatic setting of his final illness and his own spiritual and physical courage are recalled and retold by all who knew him.

Dr. Carman's most lasting contributions to our specialty have been embodied in his text on "Diagnosis of Diseases of the Alimentary Tract." From the preface to this I quote these words: "The essentials of a satisfactory roentgen diagnosis are faithfulness to an orderly routine, careful observation, cautious interpretation, re-examination of doubtful cases, and a willingness to admit, whenever it is true, that the findings are inconclusive."

I want, also, to quote a supplementary thought from the editorial introduction of an equally celebrated text in diagnostic roentgenology written twenty years later: "Even when a positive roentgen diagnosis cannot be made, information of great aid in the handling of the patient may be obtained. The importance of cordial sympathetic co-operation of the clinician and roentgenologist and a frank discussion of specific clinical problems cannot be overemphasized."

These are the words of Dr. Ross Golden, tonight's Carman Lecturer, and just as my quotation from Dr. Golden's introduction supplements that of Russell Carman, so Dr. Golden's splendid work in the field of roentgen diagnosis of the gastro-intestinal tract supplements that of the earlier master.

Dr. Golden received his early training and inspiration under the tutelage of that master teacher and beloved preceptor, Dr. George W. Holmes, later being invited to head the Department of Roentgenology in the Presbyterian Hospital of New York City. He is editor of the splendid text "Diagnostic Roentgenology," and author of the sections in it dealing with the abdomen and gastro-intestinal tract. His numerous writings have been chiefly on this important and often baffling subject, and his lecture tonight, as is especially fitting, deals with one of these problems, his subject being, "Abnormalities of the Small Intestine in Nutritional Disturbances, Some Observations on their Physiologic Basis."

ABNORMALITIES OF THE SMALL INTESTINE IN NUTRITIONAL DISTURBANCES: SOME OBSERVATIONS ON THEIR PHYSIOLOGIC BASIS

(CARMAN LECTURE)[1]

By ROSS GOLDEN, M.D., *New York City*

From the Departments of Radiology of the Presbyterian Hospital and of the College of Physicians and Surgeons, Columbia University

TO the Radiological Society of North America I wish to express my keen appreciation of the invitation to give the Carman lecture at this meeting and of the honor of the introduction by the dean of Ohio radiology, Dr. Walter C. Hill. When our President, Dr. Nichols, extended this invitation he suggested that the topic for discussion be some phase of gastro-intestinal radiology, the field in which Russell Carman was particularly interested and to which he contributed much. The subject under consideration is one in which I am sure Carman would be intensely interested, were he alive to-day, and to which a very important early contribution came from the department at the Mayo Clinic which he directed.

When the history of the present medical age is written, the investigation of the problems of nutrition will stand out as a major achievement. Much evidence has been accumulated that, even in this land of plenty, malnutrition in its various forms is far from uncommon and that its clinical manifestations are greatly varied. Numerous writers have testified to the frequency of gastro-intestinal disturbances in malnutrition. Its early recognition and correction are of great importance. To this end roentgen methods of examination seem to be making an increasingly important contribution.

In this lecture I shall attempt to discuss the disturbances in the physiology and morphology of the small intestine which are associated with abnormal nutritional conditions, and their manifestations on roentgen-ray examination. This will include a presentation of the available evidence concerning the pathologic anatomy and physiology of the intestine and an exploration of the possibilities of correlating these with the abnormalities demonstrable by roentgen methods.

The term "deficiency state" will be used in a broad sense to imply a lack of some important factor necessary for the proper functioning of the organism, for example vitamin or protein, although the exact nature of the deficiency or deficiencies may not be known.

LITERATURE

The first mention of the use of the barium meal in sprue was by Pillai and Murthi (1931) in India.[1] In American literature, Mackie (1933) mentioned abnormalities of the small intestine in a case of sprue, and Snell and Camp (1934) published a thorough study of the changes in the small intestine demonstrable by roentgen methods in a number of cases of "chronic steatorrhea." Mackie and Pound (1935) showed the same findings in tropical sprue, and Mackie, Miller, and Rhoads (1935) described them in association with severe chronic colitis. The writer (1936) pointed out similar disturbances in the small intestine in cases of infantile celiac disease.

Snell and Camp remarked that the changes they observed were probably not specific and predicted that they would be found in other conditions. As will be

[1] Delivered before the Radiological Society of North America, Cleveland, Ohio, Dec. 3, 1940.

[1] Their observations apparently were concerned largely with motility; no details concerning the appearance of the intestinal pattern were given. The number of cases is not mentioned. It seems from the description of the large intestine that some of the cases must have been chronic colitis.

shown in a later section, this prediction was correct.

TECHNIC OF EXAMINATION

Abnormalities of the small intestine in deficiency states may frequently be noted on roentgen examination for suspected disease of the stomach or duodenum, if the loops of jejunum and ileum which happen to be filled are inspected. These changes are best brought out, however, by a special examination of the small intestine which has come to be called a "small-intestine study." This consists of a series of films and fluoroscopic observation after a barium-water meal. The importance of using pure barium sulphate and water has been emphasized by Ravdin, Pendergrass, Johnston, and Hodes (1936). Pendergrass now believes that it is important to use distilled water, to avoid a possible effect from sterilizing chemicals such as chlorine, which are often present in tap water.

Details of the method vary in the hands of different workers and will not be discussed here. Our routine has been outlined elsewhere (Golden, 1936 and 1941).

CLASSIFICATION

Deficiency states have been divided into two broad groups, primary and secondary.

Primary deficiency states are those which arise apparently without obvious anatomical cause, such as celiac disease and non-tropical sprue. Possibly a chronically deficient diet may be a factor. In this group may be included cases resulting from a low vitamin intake incidental to certain therapeutic diets or to voluntary dietary restriction.

Those deficiency states are classed as secondary in which the condition is caused by, or at least associated with, disease of the gastro-intestinal tract which may interfere with the digestion or absorption of nutriment, *e.g.*, peptic ulcer, carcinoma, primary disease of the small intestine such as tuberculosis or regional enteritis, primary disease of the mesentery such as sclerosing inflammation of the lymphatics or lymphoblastoma, or biliary tract disease.

THE NORMAL SMALL INTESTINE

Recognition of the changes under discussion depends upon familiarity with the roentgen appearance of the normal small intestine. An understanding of the significance of these changes must be based upon a knowledge of the normal anatomical structure of the small intestine, an appreciation of its normal physiology, and an understanding of the available evidence concerning the pathologic changes in the intestinal wall associated with deficiency states and the other conditions in which similar small intestinal disturbances occur. Such an understanding is essential for future improvement in the early recognition of these conditions and in their differential diagnosis.

A brief summary will be given of certain facts concerning the anatomical structure and the physiology of the small intestine which have a bearing on the problem of the deficiency states.

The wall of the small intestine is composed of four coats (Fig. 1), consisting, from without inward, of the serosa, muscularis, submucosa, and mucosa. The serosa is the thin outer layer and needs no further discussion here. Lying next to the serosa, the tunica muscularis consists of an outer longitudinal layer and an inner circular layer. The submucosa is composed of very loose connective tissue containing blood and lymph vessels, which permits the mucosa to move freely over the muscularis. The mucosa consists of three parts, from without inward the muscularis mucosae, the tunica propria, and the epithelium. The epithelium is a single layer of columnar cells. Between the epithelium and the muscularis mucosae is the tunica propria, in which are loose connective tissue, wandering cells, blood and lymph vessels, and nerves, as well as occasional collections of lymphocytes. The epithelial layer can move about freely upon the tunica propria (Macklin and Macklin). The muscularis mucosae, the inner layer of the mucous membrane,

bordering the submucosa, consists of an outer longitudinal and an inner transverse layer. It extends inward in the mucosal folds (the *valvulae conniventes* or valves of Kerkring) and sends fibers through the tunica propria into the villi.

The surface of the mucosa is covered with tiny elevations from 0.2 to 1.0 mm. in height, varying in number from 10 to 40 per square millimeter, called villi. In the core of the villus is a central lymph vessel with a blind end. Muscle fibers from the muscularis mucosae extend into the villus along the basement membrane of the epithelium. Between the villi are the crypts of Lieberkühn, in which, mainly at the bottom, are the Paneth cells.

The intramural nervous system of the small intestine is complicated. Stöhr describes four systems of intramural nerves: (1) plexus subserosus, (2) plexus myentericus (Auerbach), situated between the longitudinal and circular muscle layers, (3) plexus muscularis profundus, lying within the circular muscle, (4) plexus submucosus (Meissner). These plexuses consist of networks of fibers with nerve cells, elaborately connected with one another. Auerbach's myenteric plexus is composed of three orders differing in the size of their fibrils and including two types of cells. Meissner's submucosal plexus consists of several superimposed meshworks of different structure; one lies near the circular layer of the tunica muscularis. The main plexus lies very close to the

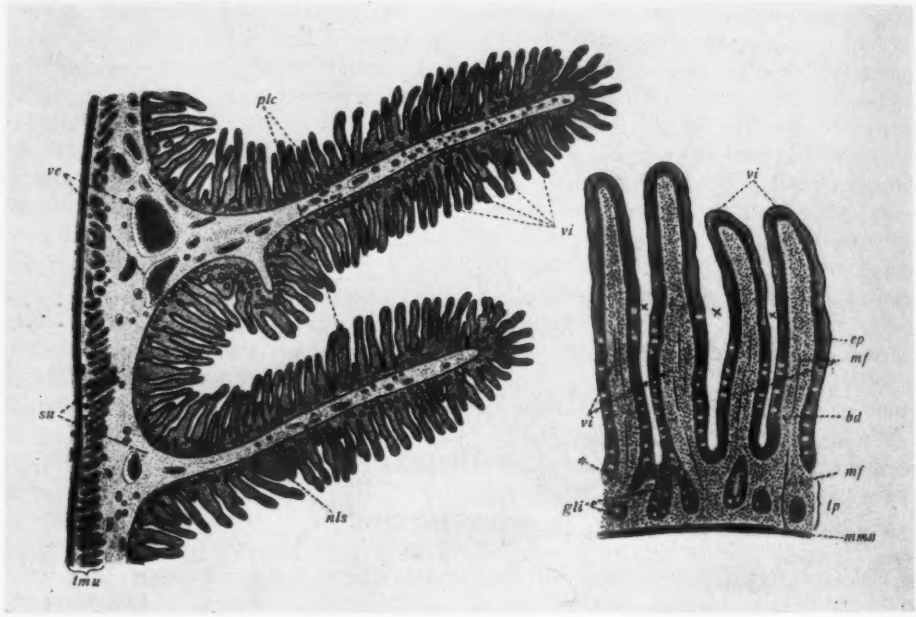


Fig. 1. The wall of the normal small intestine (from Sobotta: Atlas of Human Histology. Reproduced by permission of G. E. Stechert & Co., New York).

On the left is a low-power view of the whole wall of the jejunum. On the right is a view of the mucosa under higher magnification, showing the structure of the villi. The serosa is very thin and is not identified in this drawing. Tunica muscularis, showing the external longitudinal and the internal circular layer, *tmu*. Submucosa, *su*, containing blood vessels, *ve*. Mucosal folds, also called valvulae conniventes, valves of Kerkring, and plicae circulares, *plc*. Muscularis mucosae, *mmu*. Tunica propria, *tp*. Villi, *vi*. Muscle fibers from the muscularis mucosae extending into the villi, *mf*. According to some descriptions these fibers pass close to the basement membrane, *bd*, of the epithelial layer, *ep*. The central lymphatic or lacteal of the villus is not shown. Glands in the crypts of Lieberkühn, *gli*. A mucosal lymphoid cell collection, *nls*. The white spots in the epithelial cells are globules of mucus.

muscularis mucosae and sends fibers into this muscle and through it to the villi, the glands, and the epithelial cells.

The intramural nervous system can control all the movements of the intestine independently of influences from the extramural nerves through which it is connected to the autonomic and sympathetic systems. The myenteric is thought to control directly the muscularis, and the submucosal plexus to influence the physiology of the muscularis mucosae and the epithelium (King and Arnold).

Good discussions of the roentgen manifestations of the normal small intestine have been published by Menville and Ané (1932), Cole (1934), Ravdin, Pendergrass, Johnston, and Hodes (1936), and others. In brief, with the method we have been using, the barium shadow of the normal small intestine (Fig. 2) is usually continuous and the lumen is even in width except where a contraction happens to be taking place. The peristaltic constrictions are usually short and the wall promptly relaxes behind them. The width of the jejunal shadow averages 2.5 to 3.0 cm., and that of the ileum 2.0 to 2.5 cm. The high mucosal folds of the jejunum give the barium shadow a characteristic feathery appearance. These folds are usually 1 to 2 mm. wide and are very close to one another, 1 to 3 mm. apart. Lower in the jejunum the folds become lower and the distance between them is greater, but they are no wider. The ileal margins often appear smooth but low mucosal folds can usually be demonstrated by pressure films.

Under normal conditions the barium reaches the cecum in from one and a half to five hours, the average being between two and four hours; the ileum contains barium at six hours and is empty at nine hours. Eating is normally followed by increased motility of the small intestine; occasionally the normal ileum does not begin to expel barium until food is taken.

PHYSIOLOGY OF THE MUCOUS MEMBRANE

A series of studies on animals by von Kokas and by von Kokas and von Ludány has shown that under the stimulation of a hormone, "villikinin," the villi of the mucosal surface rhythmically shorten and lengthen, and that this pumping movement has to do with the process of absorption. It is stimulated, among other things, by the local application of yeast extract but not by pure vitamins B_1 and B_2 (Verzár and McDougall). This movement is accomplished by contraction of the fibrils of the muscularis mucosae in the villus and is controlled by the submucosal plexus (v. Kokas and v. Ludány, 1930).

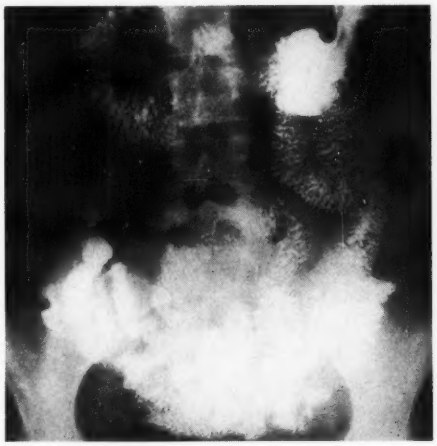


Fig. 2. The normal small intestine on the roentgenogram.

The physiology of the epithelium of the mucous membrane is very complicated, including both secreting and absorbing functions. The epithelium secretes, among other things and under special conditions, digestive enzymes, water, fat (Sperry and Bloor, 1924; Shapiro, Koster, Rittenberg, and Schoenheimer, 1936), and nitrogenous substances (Coffey, Mann, and Bollman, 1940). It absorbs all the elements of nutrition including vitamins, water, and many other things. There seems to be general agreement that absorption of fat, carbohydrates, and amino-acids is accomplished largely by means of active participation of the epithelial cells (Verzár and McDougall). Absorption is a vital function of the epithelium and not merely the seepage

of dissolved substances into the intestinal wall. Furthermore, chemical changes in the absorbed material take place within the epithelial cells, *e.g.*, the resynthesis of fat from fatty acid and the phosphorylation of absorbed material.

The presence of bile in the intestine is very important. In the absence of bile from the dog's intestine the excretion of fat is greatly increased (Sperry, 1926), the absorption of fat is diminished, the excretion of nitrogen is increased, but carbohydrate utilization is unimpaired (Coffey, Mann and Bollman, 1940).

Nerve fibers from the submucous plexus have been traced to the under margin of the epithelial cells and even between them (Stöhr). King and Arnold (1922) showed in dogs that splanchnic stimulation produces vigorous contraction of the villi in groups, and ridging and pitting of the mucosa; movements which are independent of those of the tunica muscularis; a sustained mucosal reaction is followed by the rapid secretion of mucus (suggesting that activity of the epithelial cells is directly influenced through the intramural nervous system). They state that the muscular unit of the villus is innervated directly from the submucosal plexus. It would seem probable that the function of the epithelial cells is influenced or controlled by this plexus, inasmuch as it controls the movement of the villi.

The mucosal folds of the small intestine change their form and direction under certain conditions, a fact which is familiar to all radiologists. In a loop of jejunum distended with barium, the folds lie farther apart or may be obliterated over a small area. At the site of a peristaltic contraction the jejunal folds, instead of running across the intestine, run parallel with its long axis. Similar phenomena are easily demonstrable by repeated pressure films of the terminal ileum. This change in direction cannot be brought about by contraction of the muscle coat, but must be due, as in the stomach, to contraction of the muscularis mucosae (Macklin and Macklin), which is influenced by the submucosal plexus.

The evidence suggests that the normal movements of the mucous membrane which play a part in absorption, and the normal function of the epithelium, including the actual physico-chemical process of absorption within the epithelial cells, depend upon the integrity of the intramural nervous system and in particular upon the submucosal plexus, and that impairment of this nervous system would be followed by disorder of these functions.

INTESTINAL PATHOLOGY IN DEFICIENCY STATES

Information concerning the pathologic changes in the intestinal wall in nutritional deficiencies is far from complete. Many reports give insufficient details to permit a correlation with the disturbed physiology which undoubtedly was present. Available evidence concerns largely the late stages of the disease, both in experimental animals and in patients; about the early stages little seems to be known. This is undoubtedly due in part to technical difficulties; Siegmund takes nearly a page to discuss the difficulties in the differentiation of post-mortem changes and artefacts from the true picture of the pathologic process. It is of interest that in some necropsy reports the intestine is not mentioned (Jolliffe and Goodhart; Fullerton and Innes). Holst reported a case with an apparently normal small intestine at necropsy; the patient was improving on a milk diet when she suddenly died from an intestinal hemorrhage for which no explanation could be found. It seems probable that special methods of investigation are necessary to demonstrate early or relatively slight histologic changes which may be of profound physiologic significance. The study of the intramural nerve cells, for example, which undoubtedly play a part in intestinal physiology, requires special preparation of the specimens. Lepore showed that the detection of smaller amounts of edema in the intestinal wall by ordinary histologic methods is unreliable when compared with tissue analyses for water and chloride content.

Pathologic changes in the intestinal tract in deficiency states are very variable, according to reports in the literature, both in man and in experimental animals. The available information has been summarized from necropsy reports of advanced human deficiency diseases, such as sprue and beri-beri, and from reports of animal experiments in which severe deficiencies have been produced.

Gross Pathology of the Intestine.—In well advanced deficiency states atrophy of the intestinal wall is described, varying in degree, in places amounting to gross thinning of the wall and associated with irregular dilatation. Ulcers may be present (Blumgart) and may perforate (Manson-Bahr; Fischer and von Hecker), as happened in one of our cases (Fig. 7). Congestion with hemorrhage into the mucous membrane and into the lumen has been found. The lymphoid cell collections in the wall are diminished in size but the mesenteric lymph nodes are enlarged (Whipple; Blumgart).

Pathology of the Mucous Membrane.—Atrophy of the mucosa is frequently mentioned. In two of our autopsy cases (Figs. 5 and 8) mucosal atrophy was striking; in one it was associated with obliteration (Fig. 7) and in the other with exaggeration (Fig. 4) of the mucosal folds. Edema of the mucosa is occasionally mentioned. This, as a gross observation, may be questioned, as it seems to be based upon the presence of thickened folds which, as in the case just mentioned, may not be due to increased fluid content of the mucosa but to abnormal physiology of the muscularis mucosae. In some cases the villi are shortened or obliterated. In McCarrison's experimental animals, inflammation, atrophy, and even disappearance of the muscularis mucosae were found. Degeneration of some of the fibers of the muscularis mucosae was found in one of our cases of typical non-tropical sprue (Fig. 10).

Pathology of the Submucosa.—Edema (Snell, 1939; Blumgart), round-cell infiltration (Manson; Findlay), fibrosis (Manson-Bahr), and hyperemia (Schilling) may be present in the submucosa. In one of our cases (Fig. 8) the submucosa was two to three times its normal width and was extensively infiltrated with round cells, while in another (Fig. 5) it was widened by edema. (Compare the submucosal edema in nephrosis, Fig. 15.) These submucosal changes may be of great physiologic significance because of the presence of Meissner's plexus in this layer.

Pathology of the Muscularis.—Atrophy of the muscle coat occurs in advanced cases. The reports do not mention inflammatory changes in this structure. Varying degrees of muscle fiber degeneration were found in the case of non-tropical sprue mentioned above (Fig. 10).

Pathology of the Intramural Nervous System.—Most of the reports do not mention the condition of the nerve cells of the intestinal wall, although several describe degeneration of various peripheral nerves, *e.g.*, in beri-beri (Vedder, 1913).

In his classic experiments on animals with severe dietary deficiencies, McCarrison found marked degenerative changes in the cells of the myenteric plexus; he does not mention the submucosal plexus. Etzel, a Brazilian pathologist, is quoted by de Paula e Silva as having demonstrated destruction of the myenteric plexus in the course of experiments on vitamin-B-deficient rats. Eddy and Dalldorf were unable to demonstrate significant lesions in the intestinal plexuses of B-deficient rats with polyneuritis.

A small biopsy specimen was obtained from the jejunum of one of our patients with a typical clinical picture of non-tropical sprue. The small intestine study showed the typical signs of the disease, including a smooth jejunum (Fig. 9A). A study of the biopsy specimen by Dr. William M. Rogers,[2] disclosed vacuolization

[2] Dr. William M. Rogers is Assistant Professor of Anatomy, College of Physicians and Surgeons, Columbia University. His field of research is the development and physiology of the nervous system. I am greatly indebted to him for his sympathetic co-operation.

of cells in both the myenteric (Fig. 11) and submucosal plexuses. Dr. Rogers raises the question whether cells damaged beyond repair in the course of the disease may not have been removed, leaving no trace, and whether some of the cells showing vacuoles may not recover and become normal again under continued treatment. It is of interest that histologically normal cells exist alongside of damaged nerve cells. This case proves that degeneration of nerve cells does occur with advanced deficiency disease. It seems reasonable to assume that histologic changes in the nerve cells may be preceded by a period in which their function is disturbed.

CLINICAL MANIFESTATIONS OF DEFICIENCY STATES

The clinical manifestations of deficiency states; like the pathologic changes, are variable, and their significance is often unsuspected, particularly in the early stages. They cannot be summarized here. Symptoms of some sort of digestive tract disturbance, however, are usually present, even in early cases.

Deficiency states may occur at any age, from newborn infants to the aged. Andersen found atrophy of the pancreas associated with celiac disease in the newborn, indicating that the disease was initiated before birth.

The primary deficiency conditions of the sprue and celiac disease group are usually associated at times during the course of the disease with diarrhea, with variable abdominal distress, and sometimes with an excess of fat in the stools, and rapid loss of weight. In some cases, however, no diarrhea or steatorrhea is present and the symptoms may suggest some other abdominal condition, as peptic ulcer (Case 4).

The symptoms of a secondary deficiency state may be obscured by those of the primary condition, such as chronic peptic ulcer with gastric retention, regional enteritis, ulcerative colitis, etc. On the other hand, the symptoms of a deficiency state may be the only manifestations of the primary disease, *e.g.*, lymphosarcoma of the intestine (Lehmkuhl; Golden) or sclerosing mesenteritis.

Deficiency states may be associated with any or all of the following conditions: (1) hypocalcemia, demineralization of the skeleton and even tetany (Pendergrass and Comroe; Bennett, Hunter, and Vaughan); (2) hypoproteinemia, sometimes of sufficient degree to cause edema; (3) hyperchromic anemia. In many cases, however, none of them is present.

Specific alterations in the absorbing power of the intestinal wall appear to be associated with deficiency states. Flat blood-sugar curves are consistently found following the ingestion of glucose (Bennett, Hunter and Vaughan); this is probably due in most cases to deficient absorption, as shown by Groen. Badenoch and Morris found that the blood-sugar curve rose higher after the administration of banana than after glucose in celiac disease. Gál reports a reduction in the rate of absorption of glucose to about one-third and of protein to about one-half the normal rate in vitamin-B-deficient rats; with the administration of yeast extract the absorption rates became normal.

Mottram, Cramer, and Drew (1922) showed in rats that the presence of vitamin B in the intestine was necessary for the proper absorption of fat; after irradiation with radium abnormal fat absorption persisted in spite of the presence of vitamin B. In infantile celiac disease disturbance in the absorption of fat is associated with deficiency in the absorption of fat-soluble vitamin A (Andersen); in adults disturbance in the digestion or absorption of fat, *e.g.*, from lack of bile, may produce a deficiency in the fat-soluble antihemorrhagic vitamin K (Clark, Dixon, Butt and Snell) (Case 1).

Luckner found that vitamin B_1 slowed up but did not prevent the development of edema in protein-deficient rats, while the other vitamins were without effect. He remarks that lack of vitamin B_1 hastens the development of edema through a disturbance in absorption of protein.

The condition of the small intestine,

therefore, may be part of a vicious circle which may have to be interrupted by the administration of vitamins parenterally or in excessive quantities by mouth. In some advanced primary deficiency states a permanent derangement of absorption seems to be present. Some patients must eat bananas daily to avoid a recrudescence of symptoms.

The only proof of the accuracy of a diagnosis of a deficiency state is the patient's response to specific vitamin therapy. The parenteral administration of crude liver extract, for example, is often followed by prompt improvement. Specific signs and symptoms may promptly improve when a certain vitamin fraction is injected, as, for example, nicotinic acid in pellagra. Chemical and other tests for the concentration of certain specific vitamins in the blood and urine are being developed, but opinion is not yet unanimous as to their reliability and significance. At present, good clinical judgment seems to be the best test.

ROENTGEN MANIFESTATIONS

The abnormalities of form and movement found on x-ray examination of the small intestine in deficiency states appear to be different in different stages of the disease, and even in the advanced cases they are variable. They may be conveniently assembled in three groups.

(1) *Motility*

(*a*) Hypermotility, apparently in the earlier stages (Weller; Crandall, Chesley, Hansen, and Dunbar).

(*b*) Hypertonicity, usually in the earlier stages.

(*c*) Hypomotility, in the advanced stages.

(*d*) Dilatation, particularly in the jejunum in advanced cases.

(*e*) Abnormal segmentation, that is, elongated areas of contraction, suggesting spasm, between which the lumen may be normal in caliber or larger. The contractions may be so marked that no barium remains in the contracted areas, giving the effect of scattered separated boluses.

(2) *Mucous Membrane*

(*a*) Coarsening of the mucosal folds, particularly in the duodenum and jejunum, meaning that they are wider, lower, and farther apart and, therefore, fewer in number.

(*b*) Obliteration of the mucosal folds in the advanced cases, producing a smooth wall.

(3) *Flocculation of the Barium Shadow*

This is a coarsely granular appearance, as if the aqueous suspension of barium sulphate were coarsely emulsified with some non-miscible fluid; it seems more likely to be present in the advanced cases.

In many cases gas is present in the small intestine in considerable amounts. This is interpreted by Pendergrass as an expression of the disturbance in the power of absorption of the mucous membrane. In occasional cases gas and fluid levels may suggest the possibility of ileus (Kantor).

In well marked primary deficiency states hypomotility of the stomach is frequently found. It is manifested by a six-hour gastric residue, unexplained by ulcer or pyloric obstruction, with sluggish, ineffective peristalsis, and often with antral spasm. With effective treatment the emptying of the stomach becomes normal.

In general, the disturbance in the small intestine seems to be more marked in the region of the middle third. Under treatment the abnormalities in this portion are the last to clear up and may persist when the upper part has apparently returned to normal. The terminal ileum, for some reason, except in the most advanced cases seldom appears abnormal.

In some of the milder cases, the jejunum may appear normal on the first film, whereas on the second film it shows a definitely abnormal mucosal pattern with additional evidence of abnormality, such as segmentation lower down. This change from a normal to an abnormal mucosal

pattern might be explained as a delayed abnormal response of the muscularis mucosae to the stimulus of the intestinal contents.

EFFECT OF TREATMENT

Snell and Camp (1934) remarked that the appearance of the small intestine changes *toward* the normal as a result of treatment of chronic steatorrhea. Subsequently Snell (1939) stated that proper treatment may be followed by a complete restoration to the normal in appearance. I have not seen this happen in a case of well developed steatorrhea. In a typical case prolonged treatment was followed by a return to normal caliber of the lumen, an improvement in motility, and reappearance of mucosal folds, but the folds were too low and too widely spaced to be described as normal.

Treatment of deficiency conditions in the earlier stages may be followed by a return to normal as far as the appearance of the barium shadows is concerned. A study of our cases suggests that one factor concerned is the severity of the deficiency and another is its duration. It would seem that permanent irreversible changes take place if the condition exists long enough.

Repeated studies of the small intestine during the course of treatment are instructive. By following the regression we may get some information concerning the appearance to be expected in the earlier stages and the milder deficiencies. The upper part of the intestine shows earlier

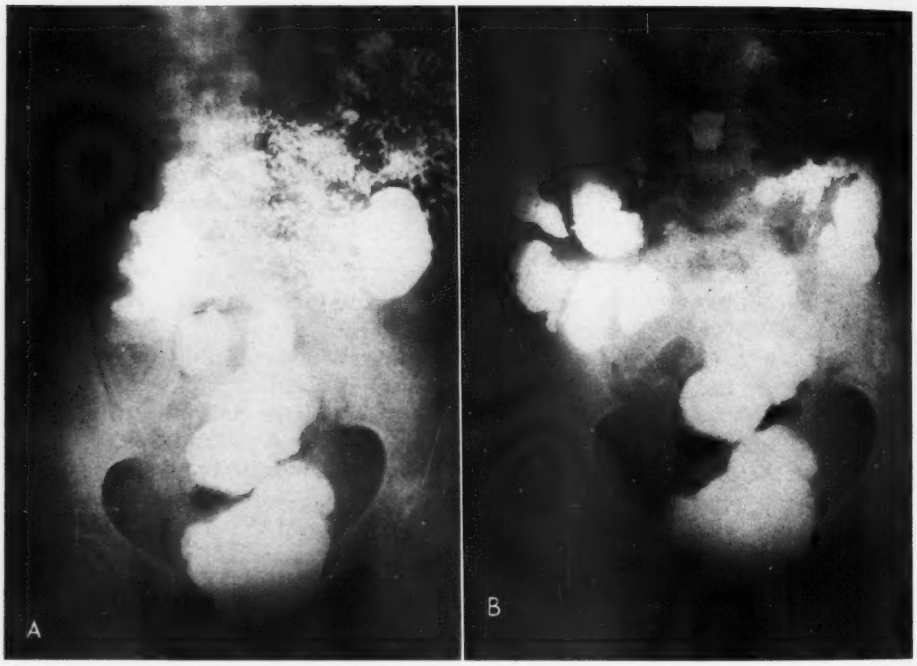


Fig. 3. Case 1: Deficiency state with atrophy of the pancreas in a 21-year-old woman.
A. Film three and a half hours after a barium sulphate-water meal shows exaggeration of the mucosal folds of the jejunum with irregularity in the caliber of the lumen. Lower down are the shadows of barium masses in the lower sigmoid and rectum from a previous barium enema.
B. Film at seven hours shows that the barium had not yet reached the cecum, indicating marked hypomotility. There is segmentation in the middle and lower loops with dilatation of those portions containing barium. See Figs. 4 and 5.

and more marked improvement than the middle part. Apparently permanent residual abnormalities may persist in the middle third after the upper part has resumed a normal appearance and after the patient is symptom-free.

Subjective improvement often follows promptly after proper treatment is begun (Fantus); one patient (Case 4) gained five pounds in a week after receiving three intramuscular injections of liver extract. Objective improvement in the roentgen appearance of the small intestine consistently lags far behind clinical improvement.

CASES

Four cases have been chosen to illustrate certain points mentioned above. Cases 1, 2, and 3 were selected because pathologic material was available. Case 4 is used to illustrate a group in which the onset of symptoms followed a nervous shock of some sort and in which the symptoms were not those usually associated with deficiency disease.

Case 1: R. G. (Unit No. 560075). A 21-year-old girl was admitted because of watery diarrhea, anorexia, gas, and loss of 30 lbs. of weight in two months. She had celiac disease as an infant, which continued to the age of seven years. She was normal except for underdevelopment until the age of sixteen, when she had watery diarrhea for a month. Following this she was normal until the onset of her fatal illness. Her diet had always been adequate. For two weeks she had swelling of the ankles, ecchymosis of the skin, and blood in the stools.

On admission the liver was enlarged. The patient had a moderate secondary anemia, hypoproteinemia, moderate hypocalcemia, a flat blood-sugar curve after the ingestion of glucose, tachycardia, and an irregularly elevated and subnormal temperature. On the ward several large intestinal hemorrhages occurred; the bleeding ceased after three intramuscular injections of vitamin K. The stools did not contain an excess of fat, as in the usual case of non-tropical sprue. A small-intestine study showed coarsening of the mucosal folds of the jejunum with segmentation and hypomotility (Fig. 3), interpreted as consistent with a deficiency state. During six weeks on the ward the patient received many intramuscular injections of liver and other vitamin B preparations without showing improvement. The tongue became swollen and sore. She continued to lose weight and died, apparently of starvation, in spite of all efforts to nourish her.

Fig. 4. Case 1: Deficiency state with atrophy of the pancreas.

At necropsy, the mucosal folds of the small intestine were interpreted by the pathologist as more prominent than usual. Compare with Fig. 7.

At necropsy (No. 12,925) no cause for the intestinal hemorrhages could be demonstrated. The mucosal folds of the entire small intestine, particularly of the duodenum and jejunum (Fig. 4) were more prominent than usual. Microscopically, the mucosa and the tunica muscularis were atrophic (Fig. 5). The submucosa was markedly widened by edema. The stomach showed atrophy of the mucous membrane and submucosal edema. The pancreas was atrophic; the islands of

Langerhans were normal. The liver was large and fatty.

Case 2: H. L. (Unit No. 589839). A 58-year-old man was admitted with a diagnosis of non-tropical sprue. He had never been in the tropics. Three years previously he had foul, foamy diarrhea for four months with loss of 10 lbs. of weight. The symptoms were relieved by diet. About one year before admission mild intermittent diarrhea began, increasing in severity during the last three months, during which he lost 45 lbs. in weight. Numerous liver injections for a month before admission had no effect on the symptoms.

On admission the patient was emaciated and had marked anemia, leukopenia, hypocalcemia, moderate hypoproteinemia, a flat blood-sugar curve after the ingestion of glucose, and elevated serum phosphatase. Roentgen examination of the intestine showed smooth jejunal loops with no evidence of mucosal folds, segmentation, and hypomotility (Fig. 6). Two injections of liver extract did no good. The patient had two chills and ran a fever up to 101°. On the eighth day he had a sudden severe pain in the left lower quadrant, relieved by a colon irrigation. On the ninth day death occurred suddenly, apparently of heart failure with pulmonary edema.

At necropsy (No. 13,177) the mucous membrane of the entire digestive tract

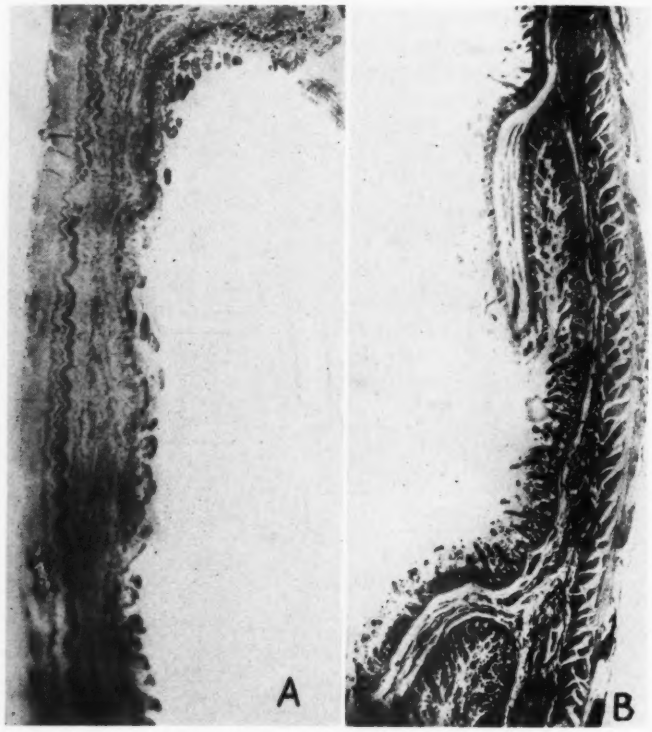


Fig. 5. Case 1: Deficiency state with atrophy of the pancreas.
A. Low-power photomicrograph of the jejunum. The epithelium is autolyzed. The mucosa is atrophic as shown by the spacing of the glands. The submucosa is widened to three or four times its normal width by edema. The tunica muscularis is atrophic.
B. Low-power photomicrograph of a normal jejunum for comparison. (Courtesy of Dr. Homer D. Kesten.)

was thin and pale. The small intestine was moderately dilated. The jejunal rugae were obliterated (Fig. 7). Scattered along the jejunum and ileum were several ulcers, 1.0 to 1.5 cm. in diameter; the base was tunica muscularis and the borders were rolled and firm. About 60 cm. from the ligament of Treitz, the largest ulcer, which encircled the wall, had perforated on the antimesenteric side; the 7 mm. hole communicated with a small abscess walled off by loops of intestine. Microscopically (Fig. 8) there was atrophy of the intestinal mucosa and of the tunica muscularis. The submucosa was widened, with round-cell infiltration and fibrosis indicating chronic inflammation, and in places with some edema.

Fig. 6. Case 2: Deficiency state (non-tropical sprue).
A film taken three hours after a barium sulphate-water meal, showing hypomotility with irregular dilatation of the jejunum. No mucosal folds can be seen.

Fig. 7. Case 2: Deficiency state (non-tropical sprue).
At necropsy the jejunum was nearly smooth. Several ulcers were found, one of which had perforated. Some of them can be seen in this photograph.

Case 3: Z. P. (Unit No. 603286). A 61-year-old man was admitted March 13, 1940, because of loss of strength and appetite and a loss in weight of 20 lbs. in six months. For two months he had nausea and vomiting. On admission he had marked hyperchromic anemia, leukopenia, an elevated red cell sedimentation rate, and anacidity. The serum protein was normal. Roentgen examination of the intestine (Fig. 9-*A*) showed a smooth jejunum with hypomotility, segmentation, and no mucosal folds. Liver injections produced evidence of improvement. After six injections an exploratory operation was performed and a small biopsy specimen was taken from the jejunum. Recovery was uneventful and the patient continued to improve under a high-vitamin diet with liver injections. Re-examination of the intestine six months after the operation showed definite improvement in appearance with the reappearance of jejunal mucosal folds (Fig. 9-*B*).

Histologic examination of the biopsy specimen by Dr. A. Purdy Stout disclosed evidence of degeneration of muscle fibers in the muscularis mucosae and tunica muscularis, and of nerve cells in the my-

enteric and submucosal plexuses. The epithelium and submucosa appeared normal (Fig. 10). Further studies with special stains by Dr. William M. Rogers, described above, confirmed the presence of vacuolization of nerve cells in both the myenteric and submucosal plexuses (Fig. 11). To the best of my knowledge this is the first demonstration of degenerative changes in the intramural nerve cells of the intestine of a patient with a deficiency state. It should be emphasized that the patient was improving under treatment at the time the biopsy was taken.

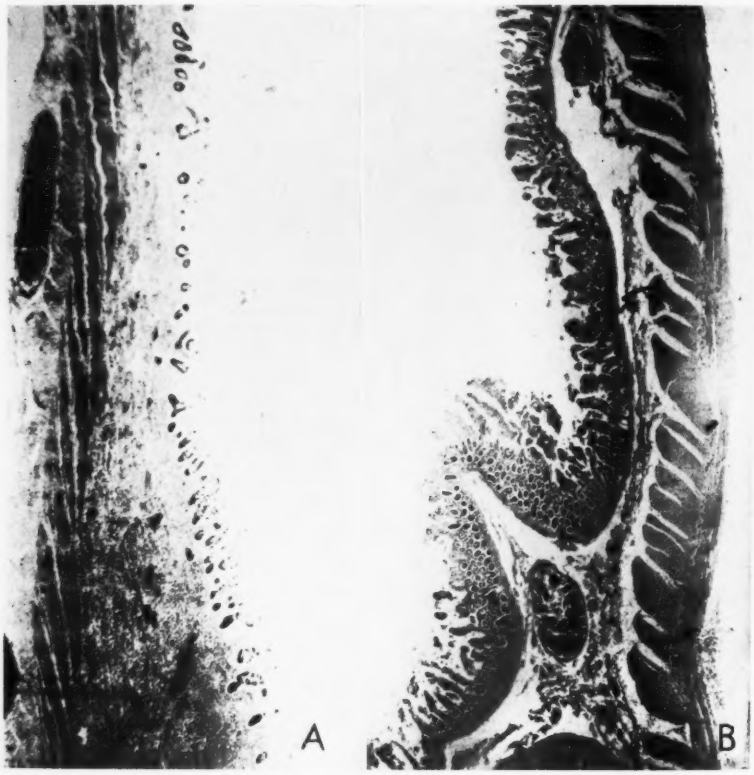


Fig. 8. Case 2: Deficiency state (non-tropical sprue).
A. Low-power photomicrograph of the jejunum. The epithelium is autolyzed. The mucosa is atrophic, as shown by the spacing of the glands. The submucosa is widened to four or five times the normal by round-cell infiltration, fibrosis and, in places, edema. The tunica muscularis is atrophic.
B. Low-power photomicrograph of a normal jejunum for comparison. (Courtesy of Dr. Homer D. Kesten.)

Case 4: S. G. (Unit No. 528757). A 29-year-old woman came to the Vanderbilt Clinic complaining of epigastric and periumbilical pain of three months' duration with a loss of 20 lbs. in weight, followed later by night sweats and increasing weakness. The onset followed an eye injury to her small son, which worried her greatly and caused her to lose her appetite. Peptic ulcer was suspected by the clinician. Roentgen examination disclosed no evidence of ulcer or of gastric neoplasm. A six-hour gastric residue was found with evidence of gastroduodenitis and antral spasm. The small intestine showed a coarsening of the mucosal folds with segmentation, interpreted as consistent with a deficiency state (Fig. 12-*A*). The pa-

tient had no diarrhea and complained at times of constipation. The stools contained an excess of fatty acid crystals but no excess of free fat. Three injections of liver extract were followed by prompt improvement and a gain in weight of 5 lbs. in a week. Re-examination of the small intestine two months later showed a definite improvement in the mucosal pattern of the jejunum. Attempts were then made for about three months to find a vitamin B fraction which might be responsible for the symptoms, but during this period the patient ceased to improve. Because of the apparent neurogenic origin of the disturbance psychiatric treatment was tried for about six months, during which the patient became worse. Re-examination of the small intestine approximately a year after her first admission showed that the "deficiency pattern" was approximately the same as at the first examination. Vitamin B complex was then given in large doses by mouth and slow but steady improvement followed. Repeated small-intestine studies showed improvement in the appearance of the small intestine (Fig. 12-*B*). Two years after admission, however, a long loop of lower jejunum showed definitely abnormal contours (Fig. 12-*C*), although the patient was clinically well. This suggests that permanent damage was done to the middle of the small intestine, although the upper part of the jejunum apparently became perfectly normal.

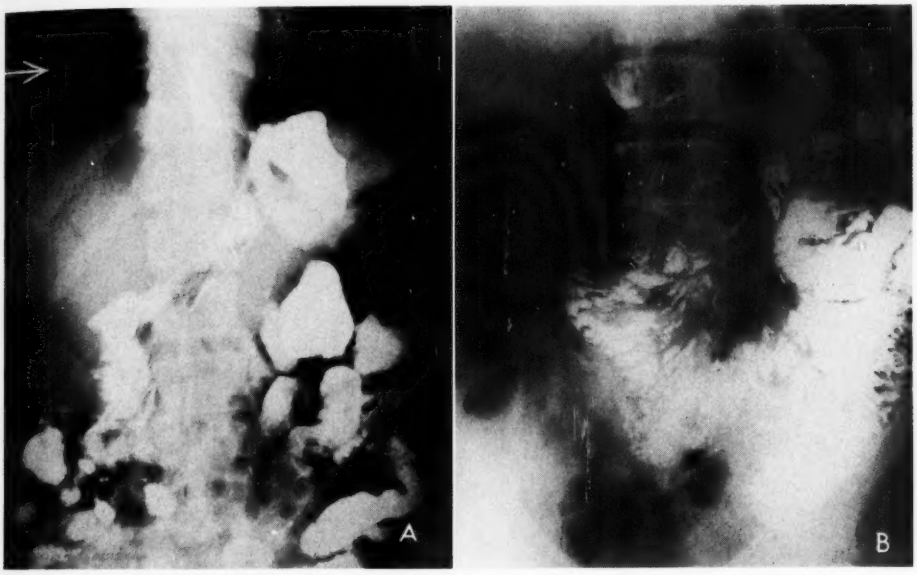


Fig. 9. Case 3: Deficiency state (non-tropical sprue).
A. Roentgen examination of intestine, March 18, 1940, before treatment, discloses hypomotility, segmentation, dilatation, and absence of mucosal folds in the jejunum. A biopsy of the jejunum was taken at this time. See Fig. 10.
B. Roentgen examination of the intestine, Oct. 9, 1940, after six months' treatment with great clinical improvement, shows some dilatation of the jejunum. Mucosal folds can be seen in places but they lie abnormally far apart. No segmentation is present. The jejunum shows evidence of improvement but is still abnormal.

The blood-sugar curves after the ingestion of glucose were flattened during the periods when the patient was worse, suggesting a slow absorption; they became normal after the administration of vitamin B complex (Fig. 13).

DISCUSSION OF CASES

In Cases 1 and 2 there was atrophy of the mucous membrane. The jejunal

folds were exaggerated in the former while in the latter they were obliterated. This emphasizes the importance of the function of the muscularis mucosae in the formation of the folds; as in the stomach, the thickness of the mucosa *per se* is not the primary factor in thickness of the folds.

Significant differences exist between the histologic appearance of the intestinal wall in Cases 1 and 2, and that of Case 3. In Cases 1 and 2 the mucosa is atrophic and the submucosa is widened by edema or round-cell infiltration; both of these patients failed to respond to parenteral liver injections. In Case 3, on the other hand, the patient was improving rapidly at the time the biopsy was taken, and no abnormality of the epithelium or submucosa could be found, although evidence of degeneration of intramural nerve cells and of muscle fibers was demonstrable. The roentgen appearance of the intestine in Cases 2 and 3 was similar, and at the time of the examination the disturbance in the function of the tunica muscularis and of the muscularis mucosae must have been much the same. I have been unable to find information concerning the time required for improvement in the histologically demonstrable disturbances resulting from deficiencies, such as submucosal edema. Fantus states that in thiamin deficiency improvement in the subjective condition and in peripheral edema, etc., is to be expected within ten days after beginning parenteral treatment. The prompt clinical improvement and gain in weight in Case 4 suggest that specific treatment was quickly followed by an improvement in the absorbing power of the intestinal wall. It seems reasonable to suspect, therefore, that submucosal edema, similar to that in Case 1, may have disappeared in the ten days of effective treatment given in Case 3.

Fig. 10. Case 3: Deficiency state (non-tropical sprue); photomicrograph of biopsy specimen from jejunum (hematoxylin and eosin stain).

The specimen was taken after the patient had begun to improve following parenteral liver treatment. The incision through the intestinal wall happened to be oblique. From left to right: longitudinal muscle, circular muscle which appears very wide due to the obliquity of the specimen to the wall, submucosa, and mucosa. The submucosa is normally narrow (compare Figs. 5 and 8). The mucous membrane, including the epithelium, is normal. Histologic study of the specimen disclosed evidence of degeneration of muscle cells in both tunica muscularis and muscularis mucosae, and degeneration of nerve cells in the myenteric and submucosal plexuses. (Courtesy of Dr. A. P. Stout.) See Fig. 11.

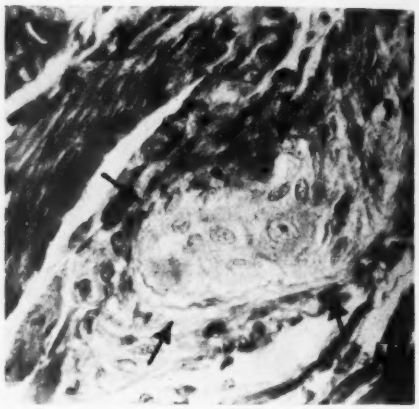


Fig. 11. Case 3: Deficiency state (non-tropical sprue); a ganglion of the myenteric nerve plexus. Photomicrograph of biopsy specimen from jejunum (trichrome stain).

The ganglion is outlined by arrows. The topmost arrow points to a nerve cell containing one large and several small vacuoles. This evidence of degeneration was found in both submucosal and myenteric ganglia in which normal appearing cells were also present. (Courtesy of Dr. William M. Rogers.)

OTHER CONDITIONS SHOWING THESE PHENOMENA

The disturbances of the small intestine described above occur in varying degrees in several conditions, as predicted by Snell and Camp.

They have been produced in dogs by a low serum protein (Barden, Thompson, Ravdin, and Frank, 1938), as well as by B-deficiency (Heublein, Thompson, and Scully, 1940). They have been seen in patients with hypoproteinemia.

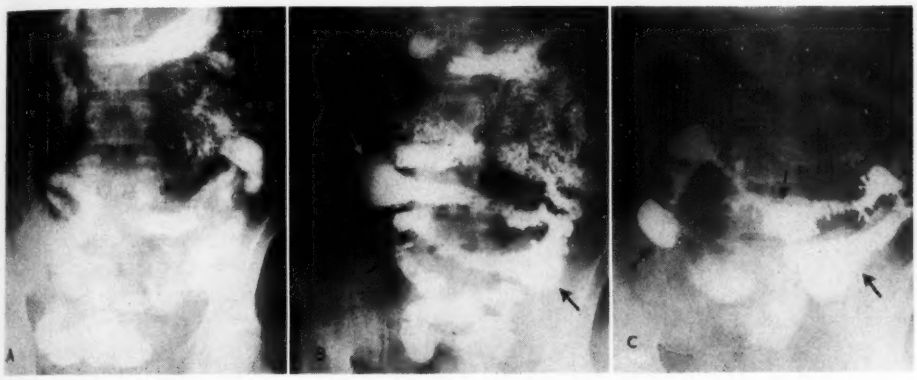


Fig. 12. Case 4: Deficiency state without diarrhea, following a period of anxiety.

A. The six-hour film following a barium-water meal on admission, Jan. 20, 1938, shows a gastric residue, coarsening of the mucosal folds of the jejunum, segmentation, and hypomotility. No barium reached the cecum in six hours.

B. The half-hour film, May 15, 1939, after about three months of adequate treatment with marked clinical improvement, shows normal motility, essentially normal mucosal folds in the jejunum, and no segmentation. The appearance of the loop of middle small intestine (arrows) is not normal in that the caliber of the lumen and the height of the mucosal folds are uneven, and two short dilated segments can be seen.

C. The one-hour film, Feb. 7, 1940, two years after the first admission, when the patient was clinically well, shows a normal jejunum. The loop of middle small intestine (arrows) appears even more abnormal than in Fig. 12-*B*. During two years this patient had fourteen examinations of the small intestine. After the symptoms were relieved this loop remained persistently abnormal, suggesting that its wall had been permanently damaged during the acute stage of the deficiency state.

They are consistently present in nephrosis (Fig. 14), as was first pointed out by Pendergrass, Ravdin, Johnston, and Hodes (1936). These workers described them also in diabetes insipidus. Nephrosis (hypoproteinemia) and diabetes insipidus are both associated with a disturbance in water balance. The edema of the intestine in nephrosis is largely in the submucosa (Fig. 15) and produces a widening similar to that observed in Cases 1 and 2 (compare Figs. 5 and 8).

Hypomotility and segmentation associated with icterus were reported by Gutzeit and Kuhlbaum (1934) and were shown by experiments on dogs and observations on patients to be due to lack of bile in the intestine.[3]

Various diseases involving the mesenteric lymphatics, which may produce the clinical picture of sprue and steatorrhea with the usual variations, have been reported by still other writers. The same roentgen picture was described by Vespignani (1925) in four patients proved at operation to have what he called "chronic mesenteritis"; steatorrhea is not mentioned. We have seen typical fatal sprue develop in non-tuberculous inflammation of the mesenteric lymph vessels and nodes (Golden, Fig. 8, 1936; reported during remission preceding the final exacerbation). In Whipple's (1907) case the lymph channels and nodes of the mesentery were

[3] Since the preparation of this manuscript a case of subacute yellow atrophy of the liver, in a man thirty-three years old, came to autopsy. Although the stools were never acholic, the intestinal tract showed definite hypomotility and segmentation, a characteristic "deficiency pattern." At necropsy (No. 13501) edema of the mucosa and submucosa of the intestine was found.

engorged with fat. Marked segmentation and coarsening of the mucosal folds were present in a case of diffuse infiltrating lymphosarcoma of the small intestine (pseudoleukemia intestinalis) with steatorrhea (Golden, 1936; Tannhauser and Davison, 1940). Lehmkuhl (1927) reported a similar case without roentgen examination. Fairley and Mackie (1937) described four cases with enlarged non-

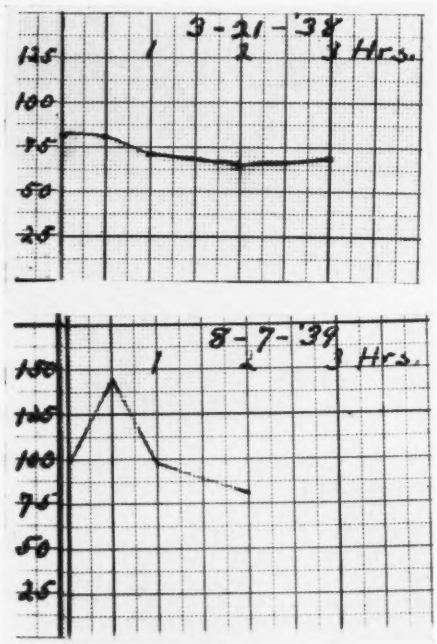


Fig. 13. Case 4: Deficiency state following a period of anxiety; blood sugar curves following the ingestion of 50 gm. of glucose in solution. Above, March 21, 1938, before adequate treatment. Below, Aug. 7, 1939, when the patient was clinically normal.

tuberculous lymph nodes, called "lymphoma," in one case with edema of the mesentery. Humphreys observed striking edema of the mesentery at operation on a patient with a deficiency state. Langmead (1937) described one case with tuberculous peritonitis. Ryle (1924) reported three cases of tuberculous mesenteric lymphadenitis (apparently without histologic proof) with fatty diarrhea, and quoted Gull (1855) as having observed fatty stools associated with disease of the mesenteric lymph nodes. Snell (1939) found one case with metastatic malignant disease of the retroperitoneal lymph nodes. Without the clinical picture of a deficiency state lymphoblastoma of the mesentery was associated with segmentation of the small intestine without coarsening of the folds in one of our cases.

Snell (1939) reported the roentgen and the clinical picture of sprue associated with pancreatic lithiasis, with carcinoma of the pancreas, and with a tumor blocking the pancreatic duct.

Wallace demonstrated similar roentgen changes in those portions of the small intestine included in the field of exposure in the course of roentgen irradiation for malignant disease in the pelvis.

Deficiency states may be superimposed upon almost any disease of the gastrointestinal tract, and may develop into the typical clinical picture of one of the well recognized entities, such as pellagra, because of obstruction or dietary restriction (Eusterman and O'Leary, 1931; Scott, 1938); the symptoms may apparently be precipitated by operation (Golden, Fig. 1, 1936). Diarrheal states (Bean and Spies, 1940) and particularly chronic colitis (Mackie and Pound, 1935; Kindschi, 1939) seem to be of importance. I have seen typical roentgen disturbances of the small intestine associated with therapeutic restriction in diet, and with regional enteritis in a number of instances; the nutritional deficiency may complicate postoperative recovery (Casten, 1939).

It is apparent that a "deficiency pattern" in the small intestine, as we have come to call it, may result from a number of causes. In many instances an actual vitamin deficiency is undoubtedly present either as a primary or a secondary factor in the picture; in either case it is of clinical importance. It is also apparent that, at least at the present time, a differential diagnosis as to the cause cannot be made from the roentgen examination alone. I believe, however, that with the clinical

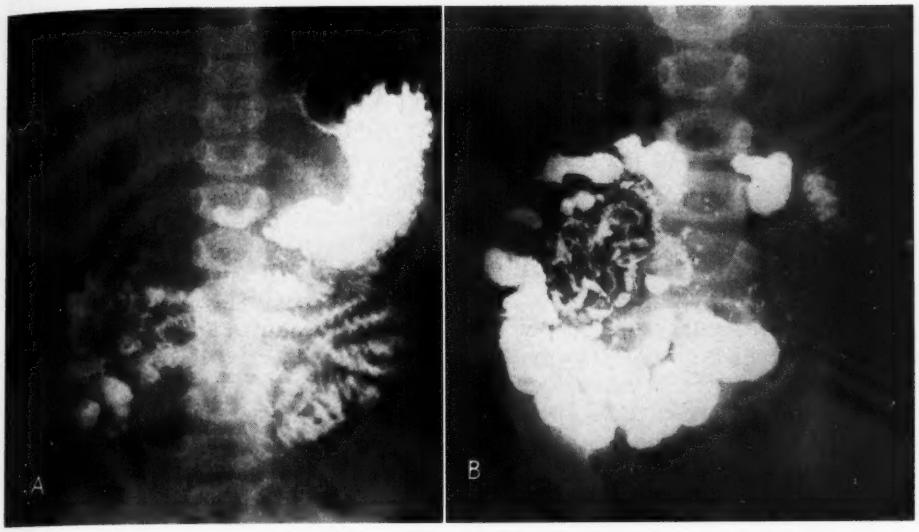


Fig. 14. Disorder of the physiology of the small intestine in nephrosis with hypoproteinemia and marked edema, in a two-year-old boy.

A. Film taken half an hour after a barium meal shows marked hypertonicity of the jejunum with coarsening of the mucosal folds.

B. Film taken two and a half hours after a barium meal shows segmentation and dilatation of certain loops of ileum and marked narrowing of others.

Within a month after this examination the patient lost practically all of his edema. Reexamination of the intestine two months later showed a marked improvement in the physiology of the intestine. In another case the disturbance in the small intestine became more marked after the edema became generalized anasarca. See Fig. 15.

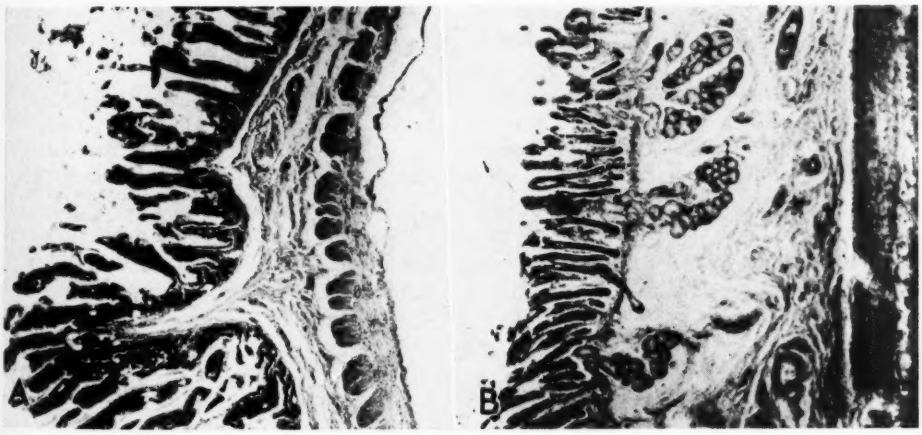


Fig. 15. Photomicrographs of the intestine in nephrosis. (Courtesy of Dr. Dorothy Andersen.)

A. Without edema. This patient had nephrosis with marked edema, from which he recovered in less than two weeks. He died about two months later from an infection. This section of the jejunum shows nothing abnormal; the submucosa is normal in width.

B. With edema. This patient died of nephrosis with anasarca. The section of the duodenum shows marked widening of the submucosa due to edema. Edema of the submucosa of the small intestine is consistently present when death occurs in nephrosis with edema.

information the significance of the findings will be clear in the majority of cases.

In 15 cases of untreated pernicious anemia in which a roentgen examination of the gastro-intestinal tract had been done to rule out carcinoma of the stomach, no suggestion of a "deficiency pattern" was visible in those portions of the small intestine which happened to be filled; the jejunal mucosal contours were undisturbed. It would appear, therefore, that the specific anti-anemic factor is not concerned directly with intestinal motility. A deficiency pattern associated with a primary anemia blood picture would suggest that a deficiency state, *e.g.*, sprue, is present, rather than pernicious anemia.

DISCUSSION OF POSSIBLE PHYSIOLOGIC MECHANISMS

The fact that the small-intestinal disturbances under discussion can be produced by such apparently different conditions as, for example, a vitamin-B deficiency, hypoproteinemia, and acholia, suggests that some common mechanism or mechanisms must be involved. Because intestinal movements are controlled or influenced by the elaborate nervous system in the intestinal wall, the possibility seems worthy of consideration that interference with intramural nerve function may be the common factor. In this connection the appearance of the barium-filled small intestine of the young infant (Bouslog and co-workers, 1935) is of interest. Roentgen examination of the intestine of the newborn (Fig. 16) differs from that of the adult in three important respects:

(1) No mucosal folds can be seen in the jejunum on roentgen examination; they appear sometime between the first and the third or fourth month. Wetzel states that in the small intestine of the newborn the mucosal folds, although present in "sufficient" number, are significantly shorter in length and height than in the adult.

(2) Marked segmentation of the barium is present, with irregularly alternating narrow and widened areas and discontinuity of the intestinal contents; three or four months later the barium shadow becomes continuous and the lumen even in caliber as in the adult.

(3) Motility is slower than in the average adult; in several infants one to three days old, examined at the Babies Hospital, the barium did not reach the cecum in five to six hours (courtesy Dr. John Caffey).

Badenoch and Morris found evidence suggesting that the absorption of glucose from the intestine, a vital function of the epithelium, is slower in the young infant than in an adult, that the height of the blood-sugar curves increases with age but the adult type is seldom found before the age of four years.

Nervous control, in general, is far from completely developed in the newborn. One logical explanation of the motility phenomena described above in the small intestine of the newborn would seem to be the lack of development in nervous control. For this reason the intestinal wall cannot react to the stimulus of its contents as it does later. Wetzel states that the mucosa in the newborn intestine is absolutely and relatively more developed than the muscle coat—the opposite of the situation in the adult. The muscularis mucosae, however, is for some reason incapable of throwing it up into folds. Unfortunately no information is available as to whether histologic differences exist between the intramural nervous system of the newborn and that of the older child. In the small intestine of the normal newborn infant, therefore, the motor phenomena of a well advanced deficiency state exist, which may reasonably be attributed to undeveloped nervous control.

Unquestionable evidence that damage to intramural nerve cells does occur in experimental and clinical advanced deficiency states has been presented above (Fig. 11). It seems reasonable to assume that a disturbance in the function of nerve cells may take place before the development of changes of a degree sufficient to be demonstrated by histologic methods, and that there may well be a much greater disturbance in intramural nerve function

than would appear to be indicated by the histologic appearance of the cells.

The pathologic changes in the submucosa—edema, round-cell infiltration, congestion, and fibrosis—may be of considerable physiologic importance. The proper function of nerve cells requires an adequate supply of oxygen and elements of nutrition. The question may be raised whether the above described changes in the submucosa would interfere with free diffusion of oxygen and other material, and thus derange nerve function.

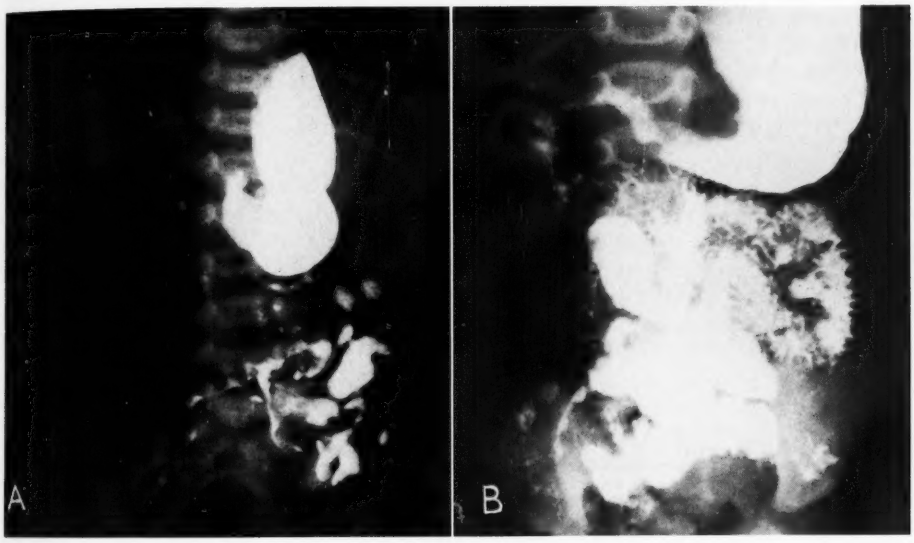


Fig. 16. The evolution of small intestinal physiology in the normal young infant. (Courtesy Dr. John Caffey.)

A. A normal infant, age two weeks. The examination was done because the patient had dextrocardia, to determine the location of the stomach. The barium is collected in irregular boluses of various sizes with narrow stretches between them. No mucosal folds can be seen in the jejunum.

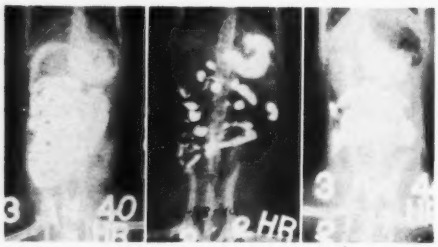
B. The same infant, age four and a half months. The lumen of the jejunum is even in caliber as in the adult. Mucosal folds in the jejunum are clearly visible, although not as high as in the adult.

The importance of vitamin B in nerve function has been well established, although knowledge of the mechanisms involved is at present incomplete. Fantus pointed out the importance of symptoms of a "neuropathy" (rather than neuritis) as one of the earlier evidences of a B_1 deficiency. In experiments on vitamin-B-deficient dogs Crandall and co-workers found that, while thiamin and riboflavin were inactive, nicotinic acid caused improvement in the disturbed intestinal pattern but was not as effective as whole vitamin B complex. All three of these fractions of vitamin B, when combined with proper proteins, form enzymes which take part in intracellular oxidation processes (Mackie, Eddy and Mills). A relation between any of them and the oxydase of nerve cells has not been traced, as far as I know, but the importance of oxidation processes to normal nerve function is attested by the number of oxydase granules in nerve cells (Kappers).

It appears that objective evidence of motor disturbances in the intestine may result from nerve impulses arising outside the intestinal wall (King and Arnold). The influence of the emotions upon the intestine is well known. A woman became emotionally upset and began to weep during the course of a small-intestine study; the small intestine, which up to that time gave the usual continuous, even-calibered barium shadow, then showed definite

segmentation. Dr. Lucien M. Pascucci[4] was making films of the barium-filled intestine of a series of normal rats. One of the animals actively resisted and showed anger by chewing continuously at the thongs. The small intestine of this rat, instead of being even in caliber as were all the others which had not resisted, showed segmentation; repetition of the procedure two weeks later without resistance on the part of the animal produced normal intestinal shadows (Fig. 17).

In view of this evidence it seems that at least one possible mechanism producing the disturbances in the small intestine in



A *B* *C*

Fig. 17. The effect of anger on the physiology of the small intestine of a rat. (Courtesy of Dr. Lucien M. Pascucci.)

A. A normal rat. The caliber of the lumen of the small intestine is even and regular.

B. A normal rat which showed persistent anger and chewed at the thongs continuously during the procedure. The small intestine is segmented.

C. The same rat as in *B* two weeks later. At this examination the animal submitted to the procedure without resistance or other evidence of anger. The lumen of the intestine is even and regular in caliber, as in *A*. At autopsy the intestine was normal.

deficiency states operates through the nervous system of the intestinal wall. If this can be accepted as a working hypothesis, the fact that the intestinal phenomena are "neither specific nor characteristic" (Snell) becomes understandable. The great variability of the motor disturbances in conditions which appear clinically identical can be explained on the basis of the degree of interference with intramural nerve function. It seems probable that more histologic evidence of nerve damage will be obtained if more care and special methods are used in the study of pathologic material. An attempt at correlation of the gross phenomena of experimental deficiencies in animals with histologic changes in the intestinal wall has not been made by most investigators.

The question naturally arises as to whether these demonstrable motor disturbances in the small intestine may reasonably be taken as indirect evidence of the probable coexistence of disturbances in other functions of the intestinal wall, such as absorption, which is also influenced by the intramural nervous system. While this question cannot be answered with assurance at the present time, the fact remains that disturbances in motility and absorption are frequently associated, and that in many cases the parenteral administration of vitamins in clinical cases appears to break a vicious circle and clinical improvement precedes objective improvement in the motor phenomena.

CLINICAL MATERIAL

In process of assembling this material the films of 75 cases were examined in which disturbances in the small intestine characteristic or suggestive of the "deficiency pattern" had been described by some member of the Department of Radiology, most of them detected during the past two or three years. At the same time abstracts were made of the patients' records. Nine of them were discarded because the changes were doubtful or border-line. Space cannot be taken here for a thorough clinical analysis, but certain facts are of interest.

Eight cases showed sufficiently marked clinical signs to permit their classification in the group of recognized clinical entities, as sprue, adult celiac disease, etc.

In three cases hypoproteinemia was considered the primary disturbance, and that was put down as the official diagnosis.

In another group the small-intestinal disturbances were associated with some well recognized disease, such as peptic ulcer (12), osteomalacia (1), acute appendicitis (1), cirrhosis of the liver (1), and

[4] Resident in Radiology, The Presbyterian Hospital.

regional enteritis (2). One patient with a typical deficiency pattern had hyperparathyroidism. Films of the gastro-intestinal tract were available in three other cases of hyperparathyroidism; although the entire small intestine could not be seen, the filled portions showed no abnormality. A re-examination three years later showed characteristic but less marked evidences of the deficiency pattern, although the patient had been given yeast extract during the preceding six months. It seems apparent that the small-intestinal disturbance in this case was due not to the hyperparathyroidism but probably to a moderate deficiency state. In one instance the deficiency pattern was associated with hyperthyroidism, while in four comparable cases of hyperthyroidism no evidence of the deficiency pattern could be found.

Fifteen cases of infantile celiac disease have been seen; in all but three evidences of the deficiency pattern were present and the three exceptions were among the earliest cases, with incomplete roentgen studies. As far as can be determined now, the presence or absence of pancreatic enzymes in the intestine makes no difference in the small-intestine pattern.

The largest group (21) was composed of patients with assorted and variable abdominal or gastro-intestinal symptoms, without any of the well recognized diseases to explain them and without sufficiently well developed and characteristic signs to justify classifying them under any of the deficiency entities. Most of the patients had one or more of the following symptoms: diarrhea, anemia, a sore tongue, variable abdominal pain, loss of weight, anorexia, nausea, etc. Two had intestinal parasites. It must be emphasized that not all patients with vitamin B deficiency have diarrhea. Many of these patients received parenteral vitamin therapy with prompt improvement. Others could not be followed. In many cases the first suggestion of the possibility of a deficiency state came from the roentgen examination; in others, this served to confirm the suspicions of the clinician.

COMMENT

As more attention is paid to the small intestine, even in routine gastro-intestinal examinations, it becomes increasingly apparent that these small-intestinal changes are to be found with surprising frequency in patients whose symptoms do not suggest any of the recognized deficiency states. Many workers on pellagra, sprue, and beriberi have pointed out that indefinite abdominal symptoms frequently occur early in the course of the disease before its outstanding characteristic manifestations appear and before a clinical diagnosis can be made (*e.g.*, Chesley, Dunbar, and Crandall). These changes are frequently found in association with common, easily recognized diseases of the gastro-intestinal tract, many of which require surgical treatment. The importance to surgeons of the recognition and the correction of nutritional deficiencies is attested by the number of articles dealing with this topic in recent surgical literature.

Experience thus far seems to justify the assumption that a properly done roentgen examination of the intestinal tract in the early stages of these diseases would in many cases disclose disturbances in the small intestine and thus draw attention to the possibility of a deficiency state before serious damage is done.

Much more work needs to be done, particularly on the pathology and physiology of the intestinal wall, before the motor disturbances and other phenomena described above can be understood. Careful roentgen observations and correlation with clinical and pathologic evidence in individual cases will assist in advancing knowledge of deficiency states and their differential diagnosis.

SUMMARY

Certain nutritional deficiency states, in both early and late stages, are associated with disturbances in the motility and mucosal pattern of the small intestine recognizable by roentgen examination. When no obvious anatomical reason for their existence is apparent they may be classi-

fied as primary; when they are associated with some organic disease of the gastrointestinal tract, mesentery, liver, or pancreas, they may be described as secondary.

Pathologic changes in the intestinal wall occur as a result of long continued nutritional deficiency, but seem to vary markedly in different individuals. There is strong evidence of damage to the intramural nervous system. The earlier changes are undoubtedly reversible, but if the condition persists long enough the intestine may be permanently damaged. Under adequate treatment the middle region of the small intestine does not seem to be restored to normal as rapidly as the proximal region; the former may show persistent evidence of damage after the latter appears normal and after the patient is clinically well.

The clinical manifestations, like the pathologic changes, are variable. The symptoms are often obscure or misleading. They may complicate a condition requiring surgical treatment.

Associated with the objective changes in the intestinal pattern, disturbances in the physiology of absorption occur which suggest that the small intestine may be part of a vicious circle, for the interruption of which parenteral treatment may be necessary.

Objective changes in the small-intestine pattern, similar to those occurring with vitamin deficiency, have been associated with clinical and experimental hypoproteinemia and several other conditions.

Exactly the same type of intestinal pattern as that found with well advanced deficiency states is present in normal newborn infants, which after three or four months is replaced by the usual adult pattern; this change is probably due to the evolution of the incompletely developed nervous control of the intestine.

It would seem that some common mechanism must operate in the production of these phenomena from so many different causes. One possible, if not the most probable, mechanism is interference with or damage to the intramural nervous system of the intestine.

Although a positive differential diagnosis cannot be made, the detection of these abnormalities of the small intestine on roentgen examination will serve to draw attention to the possibility of a nutritional deficiency and may lead to its correction before serious damage is done.

I wish to pay tribute to the spirit of cooperation which pervades the staff of the College of Physicians and Surgeons, and of the Presbyterian and Babies Hospitals. My thanks are due in particular to Dr. Dorothy Andersen and Dr. Homer D. Kesten, Department of Pathology; to Dr. A. Purdy Stout, Department of Surgical Pathology; to Dr. Elvira Goettsch, Dr. John Lyttle, and Dr. John Caffey, Babies Hospital; to Dr. William M. Rogers, Department of Anatomy; to Dr. Michael J. Lepore, Department of Medicine; and to numerous members of the Department of Radiology for their help in assembling this material.

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THE ROENTGEN DIAGNOSIS OF DUODENAL ULCER[1]

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DUODENAL ulcer is the most common lesion of the alimentary tract seen by the roentgenologist. It is with the purpose of reviewing the x-ray findings and describing my technic and procedure that I present this paper.

In reviewing some of the older textbooks on medicine, one finds that duodenal ulcer appeared in the literature as a clinical entity about 1911. This is about the time the x-ray examination of the gastrointestinal tract was developed. The roentgen findings reported at that time were corroborated by such men as the Mayos and Moynihan. But in spite of their work the importance of duodenal ulcer very slowly found its way into the literature on general medicine. In the older textbooks one finds mention of gastric and peptic ulcer but little reference to duodenal ulcer. The textbook used in some medical schools as late as 1920 (Anders, 2) had about six pages on peptic ulcer. The entire section was devoted to gastric ulcer, duodenal ulcer being mentioned only once.

Sutherland (20) states that duodenal ulcer was casually mentioned by Muralto, in 1688, but not until 1865, have we any comprehensive discussion of this subject. At this time there appeared the very excellent article of Krause. Sutherland further states that until 1914, when Cole (8, 9) directed attention to the bulbar deformity as the direct sign of ulcer, the diagnosis was based on a varying combination of indirect roentgen findings and clinical manifestations. Even after the direct method of diagnosis was well established our confreres were rather hesitant in the acceptance of this sign. It was not until the roentgenologists completely ignored the subjective symptoms and then compared their x-ray data with findings on the operating table that the present high plane of accuracy of diagnosis was attained.

Anatomically, 95 per cent of cases of duodenal ulcer occur in the bulb, usually near the lesser curvature; it is believed to occur with equal frequency on the anterior and posterior wall. It is becoming more and more recognized that the ulcer may be multiple. Chierici (7) found multiple lesions in 25 per cent of 235 cases.

As late as 1923, the incidence of duodenal ulcer was considered to be half as high as of gastric ulcer. Since that time there have appeared various estimates ranging from five times as often to ten or more times. Miller, Pendergrass, and Andrews (17) state that duodenal ulcer is four times as frequent as gastric ulcer; however, Stanley Kirkland (14) reported duodenal ulcer to be 95 per cent as frequent as gastric ulcer. My experience corresponds more to that of Kirkland than to the others.

We believe that the diagnosis of duodenal ulcer should be made by the painstaking use of both the fluoroscopic and roentgenographic methods rather than by either one alone. There does not seem to be any justification for the constant debate over which method is preferable.

Our method of procedure is as follows:

The patient reports in the morning on an empty stomach. After fluoroscopy of the chest and abdomen in the upright position, the patient is given a small amount of barium and water mixture which coats the stomach and cap. The cap is palpated and observation is made as to tenderness deformity, or other abnormalities. Films are taken in this position with and without compression. The patient is then examined in the horizontal position from various angles. One of the positions is the right oblique, with the patient lying on his back and the right shoulder ele-

[1] Presented before the Twenty-fifth Annual Meeting of the Radiological Society of North America, at Atlanta, Dec. 11–15, 1939.

vated and supported by sand bags. The patient is told to swallow air several times and films are taken in this view directly off the fluoroscopic tube. The stomach is then completely filled with the usual barium meal and observations are made as to the nature of the peristaltic waves, defects, and other abnormalities. The patient now lies on the right side for about a half hour, after which he is fluoroscoped again and films are taken on the serialograph. After about 45 minutes or an hour he is re-examined and films of the cap are taken on a serialograph with and without compression. Examination is repeated at frequent intervals until the stomach is empty.

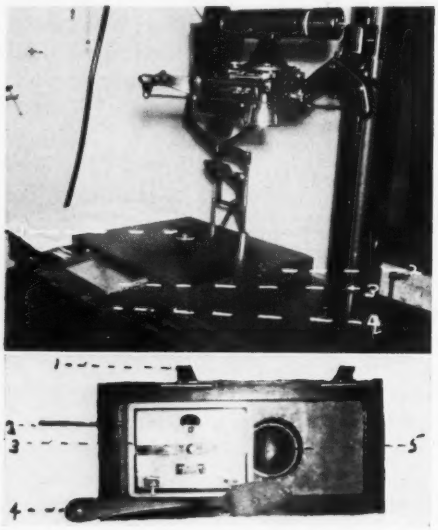

Fig. 1-*A* (*above*). (1) Hemispherical shell from spot film device used for compression in the prone position. (2) Serialograph. (3) An 8 × 10 cassette. (4) Frame which fits in the tray of the serialograph and which holds the 8 × 10 cassette.

Fig. 1-*B* (*below*). Rear view of the spot film device. (1) Hooks equipped with set screws which fit onto fluoroscopic screen. (2) Wooden plunger which moves the 5 × 7 cassette. (3) Cassette. (4) Localizer. Note lead button at center of bowl. (5) Circular opening in lead plate and rear view of shell.

In making a fairly comprehensive examination of the duodenum it is necessary to make many exposures of the cap and to use complicated equipment which is now on the market but rather expensive. To overcome this, I made some accessory devices which are rather simple and inexpensive: one permitting four views of the cap on an 8 × 10 film, and a compression spot film device that permits two views on a 5 × 7 film.

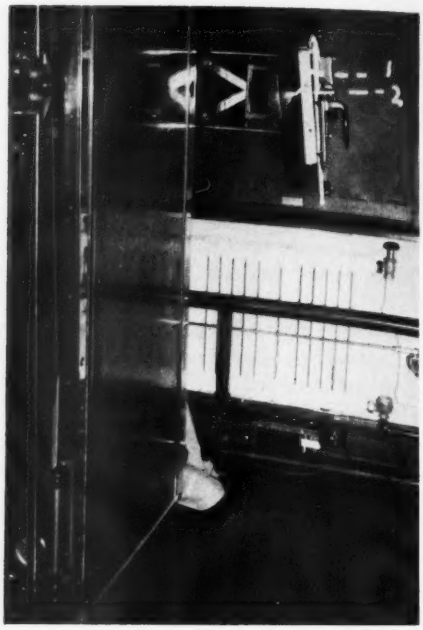

Fig. 1-*C*. Side view showing spot film device hanging on fluoroscopic screen. (1) End view of tunnel. (2) Projecting ring with hemispherical shell.

A short description of these devices is in order. The compression device consists of a simple tunnel (Figs. 1-*A* and 1-*B*), the inside measurement of which is twice the length of a 5 × 7 cassette, and the width that of a 5 × 7 cassette, backed with sheet lead. There is an opening 4 in. in diameter, the center of which is approximately 10 in. from one end and about 6 in. from the other. This is so arranged that a 5 × 7 cassette is completely covered by lead at one end. The cap is localized, and by means of a simple wooden plunger the cassette is then pushed along so that half of the cassette is exposed. It can be

pushed back and another field localized, or pushed forward for another exposure. At the front of the tunnel there is a ring projection, 2 in. in depth, on which a hemispherical wooden shell fits. This produces the compression. The tunnel is hung over the fluoroscopic screen by means of hooks which are equipped with set screws, so that the central ray strikes the exact center of the circular opening of the tunnel.

present. Aside from a deformed cap which, of course, can be seen distinctly on the film, there are noted certain secondary findings, the most important of which are hyperperistalsis and hypermotility. Many textbooks and articles state that the fluoroscopic findings are hyperperistalsis with paradoxical retention, but our experience has been that in 60 per cent or more cases of duodenal ulcer rapid emptying occurs. As a matter of fact, in cases

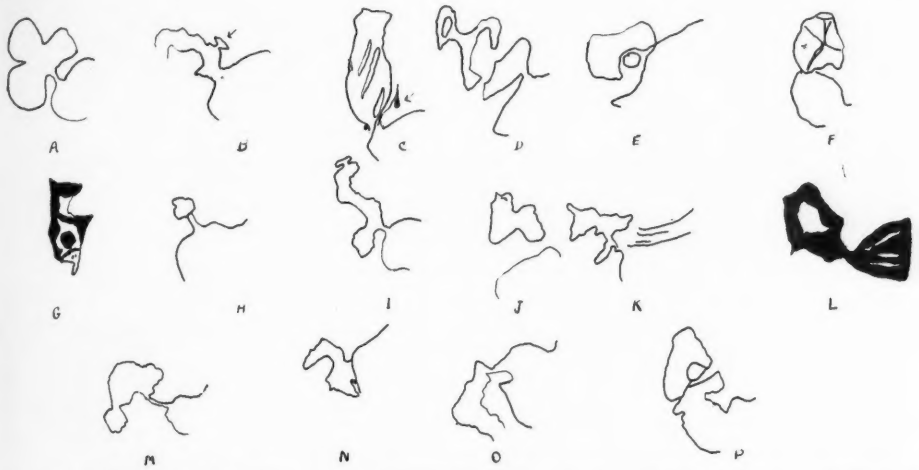

Fig. 2. (*A*) Clover-leaf deformity. (*B*) Deformity with niche *en profil*. (*C*) Niche *en profil*. (*D*) Marked deformity. (*E*) Niche *en face*. (*F*) Star-shaped folds, seen on compression only. (*G*) Niche *en face*, with marked deformity. (*H*) Phthisis bulbi. (*I*) Pseudo-diverticula. (*J*) Marked deformity. (*K*) Deformity. (*L*) Pseudo-diverticula. (*M*) Air filled cap with a niche. (*N*) Deformed cap with pseudo-diverticula. (*O*) Deformed cap with pseudo-diverticula. (*P*) Deformed cap with eccentric pyloric canal.

The serialograph (Fig. 1-*C*) is also homemade. This is the standard type on which four views on a 14 × 17 film can be taken. However, I have added a frame to the tray which holds an 8 × 10 cassette in the center and on which four views can be taken on an 8 × 10 film. For compression of the cap with the serialograph, the wooden hemispherical shell from the tunnel is used. The cap is localized over the center of the serialograph by means of a ten-cent wooden spoon through which a lead button is inserted. All this equipment was made by the building carpenter at a total cost of $15.00.

Fluoroscopic examination may reveal definite indications that duodenal ulcer is

in which there is rapid evacuation of the stomach special precautions are taken to find primary evidence of ulcer. Rigler, in his textbooks, also gives hypermotility as one of the findings. Hyperperistalsis with delayed emptying or retention occurs in from about 5 to 10 per cent of the cases and is a late finding usually present in partial or complete pyloric obstruction.

Kirklin and Burch (15) describe irritability of the bulb, which can be recognized by rapid emptying and quickly changing contour, as representing ulcer activity. Localized tenderness is found in acute cases, but is not as common as a review of the literature would indicate.

Eccentric pyloric canal and abnormal

Fig. 3-*A* (*above*). (1) Oblique view showing normally appearing well filled cap. (2) Compression view showing star-shaped folds indicating duodenal ulcer.

Fig. 3-*B* (*below*). Transition from Stage I to Stage III. (1) Roentgenogram of patient McE. (Oct. 8, 1936), showing a normally shaped cap with niche, on compression. (2) Roentgenogram of the same patient (Oct. 4, 1939) shows a contracted cap with pseudo-diverticula.

position of the bulb may be seen in the later stages, but are also seen on the film. A niche can sometimes be detected fluoroscopically and should always be looked for in order to obtain the right position and degree of pressure for a spot film.

The important roentgenographic signs of duodenal ulcer are the niche of Haudek

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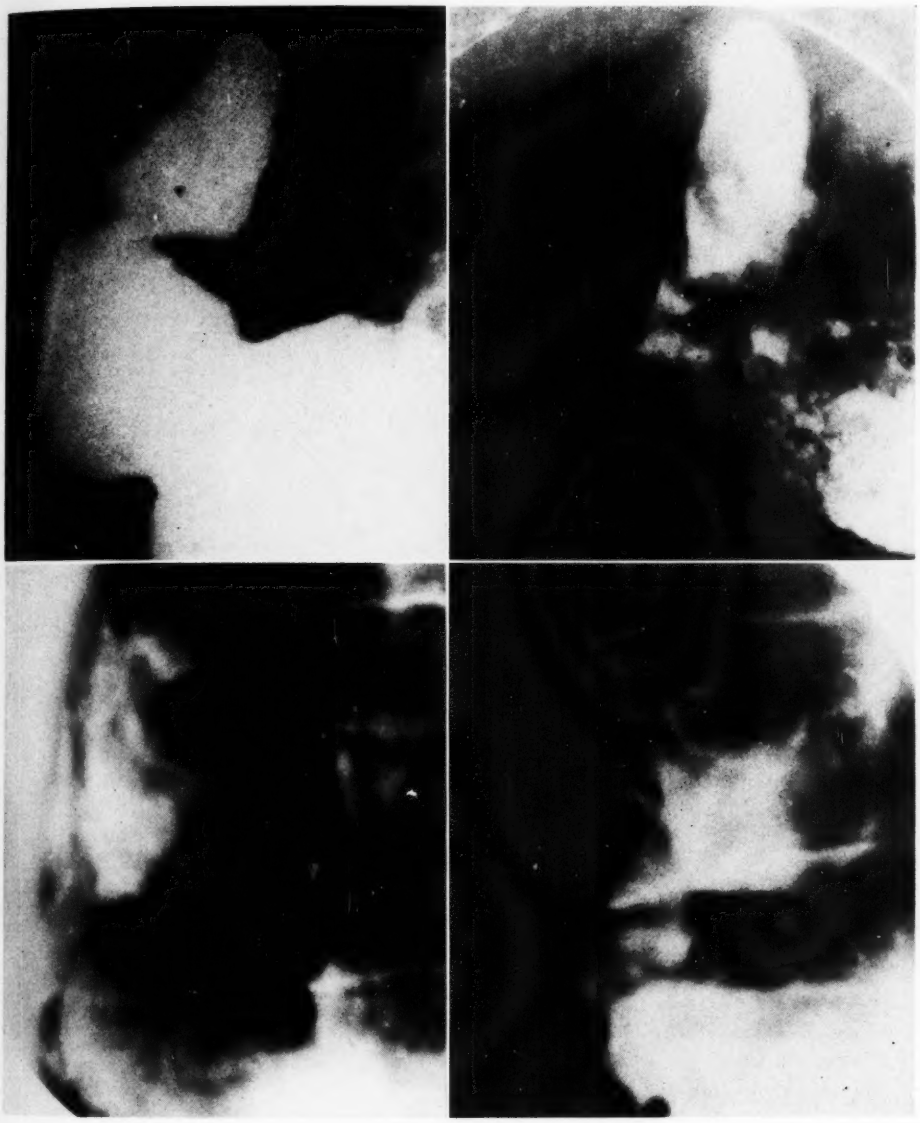

1 2

Fig. 3-*C* (*above*). (1) Normally appearing cap. (2) Compression film showing two niches.
Fig. 3-*D* (*below*). Two compression views on a 5 × 7 film. (1) Postero-anterior view. (2) Oblique view.

(13) or Åkerlund (1), as seen in Figures 2-*B*, 2-*C*, 2-*G*, 3-*C*, and 3-*D*, irregularity of shape (Figs. 2-*A*, 2-*B*, 2-*D*, 2-*J*, and 2-*N*), eccentricity of pyloric canal (Fig. 2-*P*), star-shaped fold (Figs. 2-*F* and 3-*A*), and diverticula (Figs. 2-*I*, 2-*L*, 2-*N*, 2-*O*, and 3-*B*2). Literally, the only direct sign is the niche. While the other signs are pathognomonic, they are due to secondary changes. The niche represents the ulcer crater; it is due to the adherence of the barium to the raw surface of the floor and is delineated by the

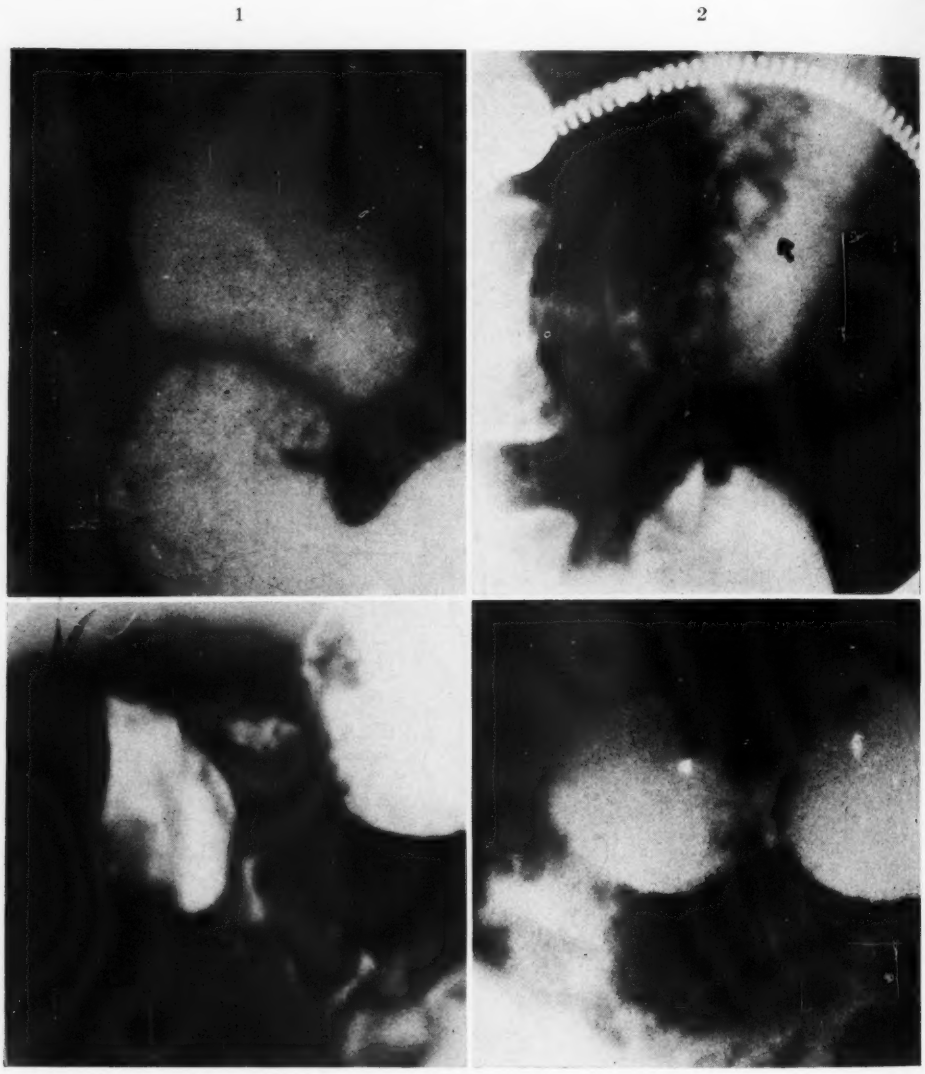

Fig. 4-*A* (*above*). Our first successful case demonstrating the usefulness of compression technic (1935). (1) Normally appearing but ectatic cap. (2) Niche on compression.
Fig. 4-*B* (*below*) (1) Niche *en profil*, exaggerated with compression. (2) Deformity of the cap at the base.

indurated rim. It was first described by Haudek (13), in 1911, and later by Lewis Gregory Cole (8, 9), in 1914, Carman (4, 5, 6), in 1916, and Åkerlund (1), in 1919. It can be seen in from 13 to 15 per cent of the cases with ordinary technic and in from 50 to 60 per cent of cases with special compression technic, and, in some cases, in the right anterior oblique position of Hampton (12) and Schons (19).

The niche is a small disc-like speck of barium, varying in size, usually 2 or 3 mm., sometimes as large as 5 or 6 mm. It has a predilection for the lesser curvature (80 per cent, according to Åkerlund) but may be found on the anterior or posterior

wall. The niches on the border have been termed "niche *en profil*" (Figs. 2-*B* and 2-*C*) and on the wall "niche *en face*" (Figs. 2-*E*, and 2-*G*). The niche must be differentiated from the pseudo-diverticula, and from a speck of barium retained within the fold. With some experience these appearances can be identified. In the early stages a niche may be seen without any other signs—except probably ectasia—which, as a rule, can be seen only by compression. Ectasia indicates an active stage of this lesion and is a valuable criterion in appraising the effect of treatment. The accessory pocket is considered to be an exaggerated niche.

The most frequent sign of duodenal ulcer is deformity of the cap. It is, literally speaking, a secondary finding and is due to a variety of factors. They are mucous membrane swelling, spasm of the muscularis mucosae, infiltration or edema of the submucosa, spasm of the muscular coats, and scarring. The chief cause of deformity is sclerosis of the wall or, as Duval, Roux, and Béclère (10) call it, rectitude of the lesser curvature. In the beginning it consists of a straightening out of the normally convex lesser curvature which may later become rectilinear or even concave. It is accompanied by a rigidity which Duval *et al.* believe is due to infiltration. Other results are disappearance of the angle between the wall and the base, gradual retraction of the most mobile portion of the wall toward the ulcerated area. Compression in this stage will show the rugæ to radiate from a point (Figs. 2-*F* and 3-*A*), the site of the ulcer.

Spasm of the muscularis mucosae and of the muscle proper contributes its share of the deformity. The defect is produced opposite the ulcer and, therefore, is usually on the greater curvature side. In some cases it is only a small concavity, in others it is a large incisura, and, in still others, it is so great as to reduce the caliber of the lumen to thread-like proportions. The deformity may be relieved but not completely obliterated by antispasmodics. That the deformity is due to spasm accounts for the fact that it frequently cannot be seen at the operating or post-mortem table. Sometimes the deformity is concentric in character and so great that the cap is reduced to about the size of a pea (phthisis bulbi, Fig. 2-*H*).

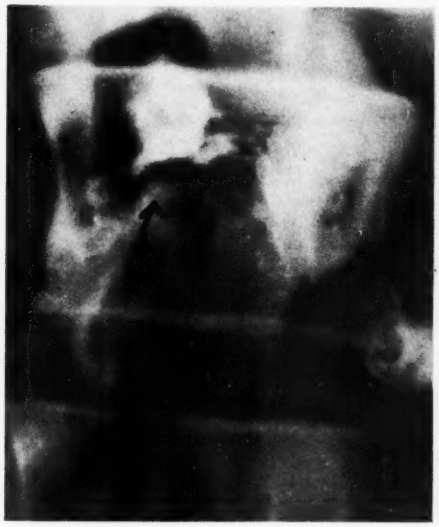

Fig. 4-*C*. Air-filled cap showing niches.

In later stages the contraction is so great that pseudo-diverticula are formed (Figs. 2-*N* and 2-*O*). When in these later stages, the sclerosis has gone beyond the limits of the ulcer and the lumen is changed to a rigid canal, the pressure of food tends to enlarge the uninvolved wall, producing diverticula. Martinotti (16) distinguishes six varieties, depending on the site of the ulcer, as follows: (1) a rigid canal with diverticula from a juxtopyloric ulcer; (2) a rigid canal with only one basal diverticulum due to a basal parapyloric ulcer—the diverticulum being opposite the site of the ulcer; (3) a rigid canal with two diverticula at the base—one to the right and one to the left—due to parietal ulcer in the middle; (4) a rigid canal with two diverticula on the same side caused by a parietal lateral ulcer of the middle portion; (5) a very rigid canal which is wider toward

the base, due to a parietal distal ulcer, and (6) a rigid canal with multiple diverticula which may or may not be symmetrical.

Sometimes we see eccentricity of the pyloric canal. This may be due to different causes, such as adhesions, a niche near the greater curvature pulling on the pylorus, pericholecystic adhesions, or congenital abnormalities. Because of the variety of causes, this sign has no value if seen by itself.

Martinotti (16) recognized three stages in the development of ulcer and believes that the signs appear in definite sequence in keeping with the stage of the ulcer.

First Stage.—Initial ulcer with or without sclerosis. A niche *en face* or a niche *en profil*. To this may be added ectasia without deformity but with a niche.

Second Stage.—Ulcer with definite area of sclerosis. Rigidity of the walls. Eccentricity of the bulb. Pseudo-diverticula.

Third Stage.—Results of sclerosis. Rigidity of the canal with or without diverticula (Fig. 3-*B*).

There are various conditions other than ulcer which will produce deformities of the cap. Pericholecystic adhesions will cause the bulb to be irregular, but the irregularity is not constant. As a rule the cap will be angulated upon the pyloric end of the stomach. Spasm of the duodenum caused by extraduodenal lesions may produce a defect similar to ulcer but can be ruled out by the administration of 1/50 gr. atropin sulphate administered hypodermically or 5 mg. of benzidrine sulphate administered orally. One must be sure that the deformity is not due to peristalsis or to incomplete filling. To obviate this it may only be necessary to have the patient lie on his right side for from one-half to one hour. Another point of diagnosis is to avoid mistaking the pyloric end of the stomach for a well filled cap, or a dilated pouch of the second portion of the duodenum for a normal appearing bulb. Experience is the only safeguard in this respect.

Because this discussion is limited to duodenal ulcer, I do not wish to leave the impression that it is good policy to limit the examination to just the stomach and duodenum. In 1927, Arens and Bloom (3) demonstrated the frequency of multiple abdominal lesions and found that duodenal ulcer without other lesions occurred in 34.5 per cent of cases and probable uncomplicated ulcers in 9.4 per cent, while in 56 per cent of the cases the ulcer was associated with other gastro-intestinal conditions.

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DISCUSSION

MILTON J. GEYMAN, M.D. (Santa Barbara, Calif.): Roentgenographic niche visualization is the most reliable sign of duodenal ulcer. While large ulcers with sharply contracted bulbs will often show crater outlines, particularly with the rotating anode tube, most duodenal ulcers will require some form of compression for positive crater identification.

It makes no great difference what you use for a compression medium; it is important how you use it. The compressor Dr. Bloom has shown will serve as well as the more elaborate devices now available.

The only advantage the larger units have over simple ones is that they permit fixation of the patient, advantageous particularly when films are desired in Åkerlund's second oblique position—an excellent position to differentiate between posterior and anterior wall lesions.

Compressors of the type mentioned are practically useless when the patient is placed in the prone position, and in this position the inflation type, such as the old Chaoul compressor, is contra-indicated because there is the danger of rupture in a perforating type of ulcer. For this position we like the wooden blocks, recently described by Hershonsen, about a year ago.

Niche visibility is not only important for original diagnosis, it is invaluable objective evidence for comparison with periodic studies to show response of a lesion to treatment. Dr. Bloom mentioned his niche incidence as being 60 per cent. I think that is a good incidence to start with. I think if we start with 60 per cent, we are showing a good many craters. As we continue to use this compression technic, however, I think our niche incidence will rise. Åkerlund right now has an incidence of between 75 and 80 per cent, which is the highest reported. Our own does not run that high; 65 per cent is the best we have been able to do. We are, however, quite critical as to what we regard as niche evidence.

Crater obliteration occurs more slowly in duodenal than gastric ulcer. We suggest that a check be instituted in the case of bed patients three weeks after treatment, and five or six weeks after in ambulatory cases.

As regards multiple duodenal ulcers, we do not see them often. When we do they are "kissing ulcers" as originally described by Moynihan. They are shown only in good compression films. We find coexistent gastric and duodenal ulcer to be more common than several duodenal ulcers.

There is one type of ulcer which I believe deserves mention. That is the apical lesion. It is easily overlooked. It shows best in screen study with the patient in a right oblique erect position. It can be shown without compression but it shows to better advantage when some compression is used. It is usually of larger size than the lesions seen in the mid-portion of the bulb and is apt to show a wider zone of edematous mucosa around the crater.

This type was described some twenty years ago by Forssell and still stands as presenting an edematous zone of mucosa around the ulcer. Such a lesion in the apical portion of the bulb seems to be a little larger as to crater size.

There is one type of patient in whom it is well to have adequate roentgenographic evidence of the mucosal structure, even though it is essentially normal. This is a patient who has a history compatible with ulcer but shows no evident gastroduodenal lesion—perhaps an irritable bulb but no fixed deformity, and insufficient transient deformity to qualify as the duodenitic bulb described by Kirklin.

This type of patient with persistent symptoms may develop a frank ulcer, well shown by some subsequent roentgen study. With conventional films of a filled normal bulb, one might feel that a crater had been overlooked during fluoroscopic study; with films of a thinly filled cap, one at least knows that no visible crater fleck was present. But it gives us considerable assurance to go back to the first examination if we can show really adequate mu-

cosal structure with various degrees of compression.

As to the second case which Dr. Bloom showed, with the niche at the base of the bulb in the so-called "superior recess," according to Forssell's nomenclature, I think we ought to be careful about calling such lesions niches. This type has bothered me no end, and I rather hesitate to call it an ulcer. This is such a favorite site for a small accessory pocket, especially tiny ones, that radiologists should avoid the error of a false interpretation. Dr. Cole drew my attention to this danger some years ago, and I think that his criticism was justified.

EDWARD L. JENKINSON, M.D. (Chicago): Dr. Bloom spoke about the time consumed completing his examination. I know that he is especially thorough, but if from a half to three-quarters of an hour is consumed doing this, I think in a large department there would be a good deal of trouble getting through with the work. I am not criticizing this; I think it is a fine way to do, but I believe that most of this work can be done in less time.

Regarding the niche, I think he has brought out here quite definitely the importance of compression. What type of compression is used is, of course, a matter of personal opinion and ease of application. In our department, we are using a compressor which was brought out by Dr. Potter a number of years ago, consisting of only a ring and a balsa-wood compressor. It can be made any shape desired. I think it is helpful if the upper part of the compressor is cut off so it conforms to the shape of the costal margin. In that way it does not hurt the patient, and I think it is possible to reach up under the costal arch and compress the bulb in a great many instances in which it would not be possible to do so with just a round compressor.

As Dr. Geyman brought out, the importance of an irritable bulb should be emphasized. Personally, I do not believe that we find craters in all ulcers. I think a 60 per cent incidence is about right, but I feel quite confident that there are patients who have symptoms—definite symptoms—referable to the duodenal bulb but who show no niche.

I know that in reviewing the cases in which symptoms continued after we had said that no duodenal ulcer was present, we discovered that our sole finding was an irritable bulb, which has a tendency to remain empty in the presence of symptoms. I think if such patients are allowed to go untreated, later on many of them develop ulcer craters. If you find a definite irritable bulb and you can rule out gall-bladder and other extraduodenal lesions which might cause this irritability, I can see no reason why the patient should not be placed on duodenal management, and I think in some instances the chance of developing a crater will probably be obviated.

There is one more thing I wish to mention. A great many heavy muscled men show a definite concavity at the base of the duodenal bulb. Much has been written about the significance of this concavity. It is our opinion at the present time that this concavity is probably due to pressure from the pylorus, and is usually seen in the recumbent position. In fact, it is infrequently seen in the upright position. The patient with the stomach in the transverse diameter of the abdomen and a high duodenal bulb is quite apt to have a concavity at the base of the bulb, especially if the peristaltic waves are rather active. It is also thought that the concavity at the base of the duodenal bulb is due to a large pyloric sphincter. I am inclined to believe that this also may have something to do with the deformity.

ARTHUR R. BLOOM, M.D. (*closing*): I may add that I agree perfectly with Dr. Jenkinson in his idea about the irritable bulb. The question was asked, "What is meant by an irritable bulb?" It is one with such rapid emptying and filling that it is impossible to get a filled bulb at any time.

DUODENAL DIVERTICULA[1]

By SYDNEY WEINTRAUB, M.D., *and* ALLAN TUGGLE, M.D.,[2] *New York City*

From the Departments of Radiology of New York Hospital, and Cornell Medical School

IN this study of 310 cases of duodenal diverticula we have not only considered the radiologic aspects of the subject but we have also attempted to evaluate their clinical significance. No doubt every radiologist has had the following experience. After completing a gastro-intestinal series the only positive finding may be a diverticulum of the duodenum. The clinician will then want to know whether or not this pocket is the cause of the patient's symptoms, which may vary from mild indigestion to severe pain with vomiting or even hemorrhage. It is mainly to answer this question that we are presenting these data.

Roentgenographically diagnosis should not be very difficult. The diverticulum is characterized by an extraluminal collection of barium communicating with the main duodenal stream by a stem of varying size. The pocket may be a few millimeters in size or, as Lockwood (1) reports, may become so huge as to contain 1,000 c.c. of fluid. Two of the largest in our series measured 7 cm. in diameter. They may arise from any portion of the duodenum, most frequently from the internal or pancreatic border but occasionally from the external border or from the anterior wall. The mucosal pattern of the adjacent duodenum reveals its normal markings, but at the stem of the diverticulum the mucosa assumes a linear pattern. This aids in distinguishing it from benign or carcinomatous ulceration. The pocket itself occasionally may show poor quality, due to the displacement of the barium by food or mucus; and at times, in the vertical position a fluid level can be seen.

The fact that approximately one-half of the lesions were not seen fluoroscopically is not of great significance, because in a teaching institution the examinations are performed by men of varying degrees of experience. In this connection it is interesting to note that we can usually gauge the ability of our residents by the number of diverticula which they discover fluoroscopically. Generally the lesions are found in proportion to the care with which the fluoroscopy is done. However, this statement must not be taken too dogmatically, because on several occasions, although the pocket was known to be present, a search by an experienced fluoroscopist failed to reveal it. In one instance a diverticulum was not seen on three different radioscopic examinations and was noted on only one of the sets of films. In another instance the pocket was not seen either fluoroscopically or on the films on two successive examinations. On the third examination it was visualized both roentgenoscopically and roentgenographically and there was a six-hour retention in the pocket. However, a fourth and fifth examination again failed to reveal the diverticulum.

DISTRIBUTION

There was a total of 349 diverticula, which included some instances of multiple pockets. The majority, 231 (66 per cent), arose from the inner border of the second portion of the duodenum, which is in accord with the findings of other investigators (2). This predilection of site is explained by Boyd (3) as being due to a weakness of the inner and posterior aspect of the gut because the vessels enter at this point. He also likens the diverticulum to an aneurysm, in that it is produced by a weakening of the wall, together with an increase in pressure within the bowel. Thus the pocket protrudes through the true mus-

[1] Presented before the Twenty-fifth Annual Meeting of the Radiological Society of North America, at Atlanta, Dec. 11–15, 1939.

[2] Present address, Charlotte Memorial Hospital, Charlotte, N. C.

cular coat and is composed of mucosa and muscularis mucosae. Others (4 and 5) have found aberrant pancreatic tissue within the wall of the duodenum, thus producing a mural weakness; and some have ascribed the occurrence of these pockets to a developmental defect in the wall adjacent to the entrance of the pancreatic and biliary ducts.

The distribution of the remainder of the diverticula was as follows: six (1.7 per cent arose from the inner border of the first portion of the duodenum. (We have excluded the so-called pseudo-diverticulum of the cap secondary to duodenal ulcer.) Forty-nine (14 per cent) arose from the inner border of the third portion; 37 (10 per cent) arose from the inner border of the fourth portion; 17 (5 per cent) arose from the outer border of the second portion; 5 (1.4 per cent) arose from the anterior wall of the second portion; 3 from the outer border of the third portion, and 1 arose from the outer border of the fourth portion.

Fig. 1. A single diverticulum arising from the second portion of the duodenum, showing parallel pattern of mucosa in the stem of the pocket.

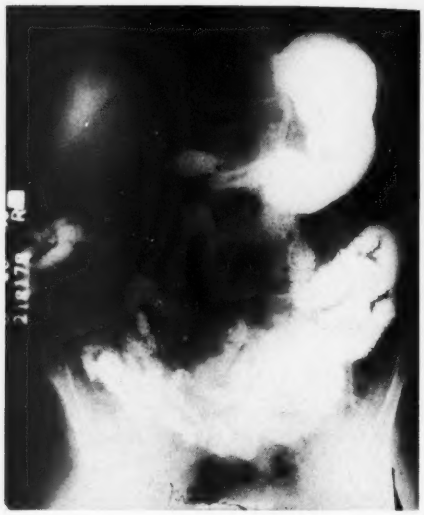

Fig. 2. Diverticulum of the third portion of the duodenum showing a similar mucosal pattern.

In 52 cases there was a six-hour retention of barium in the pocket and in 13 other instances there was a 24-hour retention. At no time did we find either gallstones, ulcer, or carcinoma in a case of diverticulum.

A review of 4,400 consecutive gastrointestinal series by Rude (6), of this Department, showed the presence of duodenal diverticula in 104 cases, an incidence of 2.4 per cent.

It has been our impression that if one congenital defect is found in the gastrointestinal tract, others are likely to be present. This has been borne out first by studying the frequency of diaphragmatic hernia, *i.e.*, the short esophageal or congenital type, as it occurred in this series of duodenal diverticula. Diaphragmatic hernia was present in 9 per cent of our cases, whereas a review of the 4,400 examinations mentioned above revealed an incidence of only 2 per cent. The impression is further confirmed by noting the occurrence of diverticula of the colon in our cases. The colon was examined in 193 instances either by barium enema or by a 24-hour observation. Of these, 45 (23 per cent) revealed the presence of diverticula, whereas the usual incidence as reported by most authors (7) is 10 per cent or less.

Some of our cases showed a multiplicity of congenital defects, as follows:

Hernia, duodenal and colonic diverticula 10

Diverticulosis of the esophagus, duodenum, and colon..... 2
Hernia and diverticulosis of the esophagus, duodenum, and colon..... 1

Among the associated pathologic lesions in the upper abdomen, there were 40 duodenal ulcers, 36 pathologic gall bladders, 6 gastric ulcers, 6 gastric carcinomas, and 3 cancers of the pancreas. The fact that diverticula of the duodenum occurred in the older age groups would explain this rather high incidence of upper abdominal

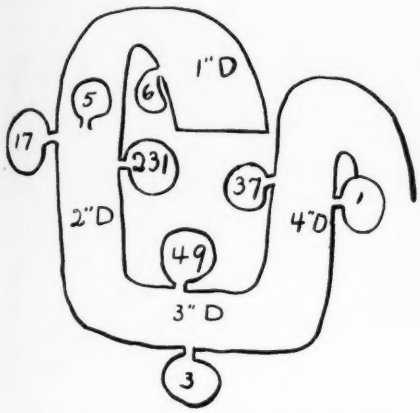

Fig. 3. Anatomic distribution of the diverticula in the duodenum.

pathology. We do not believe that there is any causal relationship.

TABLE I.—CLINICAL DATA

Age	Male	Female
11–20	0	1
21–30	7	1
31–40	20	23
41–50	31	40
51–60	50	58
61–70	23	35
71–80	8	11
81–	2	0
Total	141	169

The distribution among the sexes was about equal. As seen in Table I, the incidence is higher in the older age groups, though we had nine cases below the age of 30 years, the youngest being 18.

SYMPTOMATOLOGY

We assumed that if a diverticulum were diseased and producing symptoms, it should show one or more of the following signs roentgenographically:

1. Localized tenderness.
2. Changes in the mucosal pattern of the diverticulum, such as a persistent fleck.

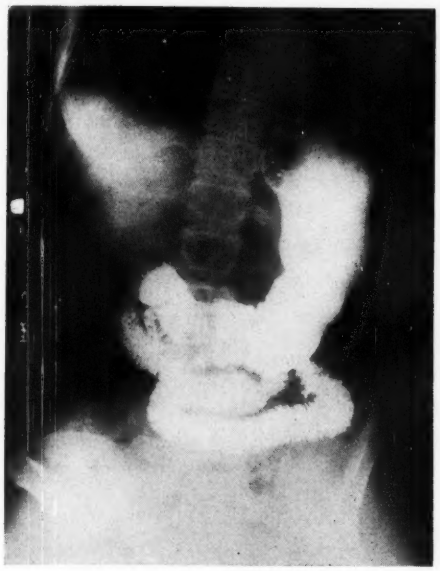

Fig. 4. Diverticulum in the lower second portion of the duodenum, showing poor quality due to retained food or mucus.

3. Mucosal changes of the adjacent duodenum.
4. Irritability of the duodenum.
5. Stasis in the duodenum.

In only four cases were any of the above signs present and in these tenderness was the only sign. However, we could not see any causal relationship between the symptoms and the diverticulum in any of these cases.

Case 1. A female, aged 39 years, had had her gall bladder removed nine years previously. Recently she had two attacks of acute colic in the right upper quadrant, lasting from 10 to 20 minutes. There was no jaundice. Probable diagnosis was recurrent biliary calculi.

Case 2. A female, aged 74 years, had as her chief complaints belching and pain in left upper quadrant. She had passed

a urinary calculus some years previously. X-ray examination showed left renal calculus.

Case 3. Male, aged 30 years, had had epigastric pain for three weeks, relieved by food; also some belching and distention. There had been no nausea or vomiting. The patient was on Government relief and requested additional allowance for special diet. The Wassermann test was 4+. One year later, according to notes in syphilis clinic, the patient stated that he had had no gastric complaints in the past year.

not improve on an ulcer régime. Surgical treatment was not believed to be indicated in any of these.

Three cases were operated upon primarily for the diverticulum. Roentgenographically, however, we did not feel that the patients' symptoms were due to disease within the pocket. In two of these the pathologic examination showed no evidence of inflammation; the third revealed a mild chronic inflammatory reaction. This patient, however, had had a cholecystectomy two years previously, at which time the pocket was seen but not

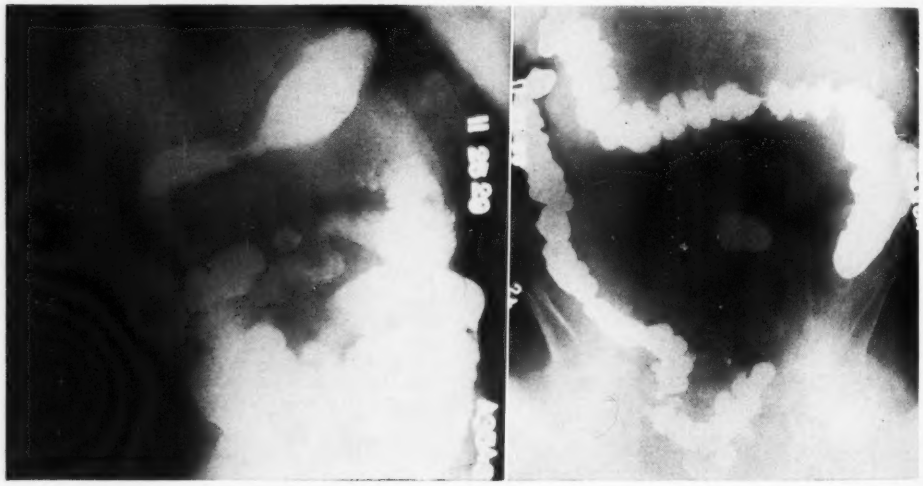

Fig. 5. Associated duodenal diverticula, colonic diverticula, and diaphragmatic hernia. Twenty-four-hour retention in duodenal pocket.

Case 4. Female, aged 47 years, complained of bloating, fullness, dizzy spells, flushes, tired feeling, and constipation of two years' duration. Psychiatric consultation: menopause, psychoneurosis, and a tendency to magnify complaints.

There was another group of 11 cases in which, if one is liberal in the interpretation of the history, one might assume that the diverticulum was the cause of the symptoms. However, in none of these was there any roentgenographic evidence of inflammation. The history in these cases was more or less typical of ulcer but it is noteworthy that these patients did

removed; she returned complaining of pain in the right upper quadrant and at the second operation numerous adhesions were found and the pocket was removed. Three years later her complaints were unchanged.

Fourteen of our cases had postmortem examinations, in none of which was there any evidence of pathology in the diverticulum.

From an analysis of the clinical data we feel that it is very hazardous to assume that a diverticulum is the cause of abdominal symptoms. There apparently was no definite proof in any of our cases

that the diverticulum was really the offender, in spite of the fact that many had a six- or twenty-four-hour retention of barium.

CONCLUSIONS

1. Among 310 cases of diverticulosis of the duodenum we found a much higher incidence of diaphragmatic hernia than occurred in an unselected series of gastrointestinal examinations.

2. From the clinical aspect we could not say in a single case that symptoms were caused by pathologic changes in a diverticulum.

3. The pathologic examinations of the diverticula in 14 autopsies and in three surgical specimens showed inflammatory reaction in only one and in that case the changes were probably secondary to other lesions.

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DISCUSSION

B. R. KIRKLIN, M.D. (Rochester, Minn.): I have nothing to add to the authors' paper, as I agree with them when they say that duodenal diverticula are common, have little if any significance, and seldom, if ever, warrant surgical intervention.

In my opinion, their presence should not be regarded too seriously and their diagnosis is of value chiefly as evidence that the radiologist has examined the duodenum with care.

JOHN MARSH FRÈRE, M.D. (Chattanooga, Tenn.): It is a little off the subject but I should like to ask Dr. Tuggle if he discovered any diverticula of the appendix in his series.

ALLAN TUGGLE, M.D. (*closing*): I have not seen a diverticulum of the appendix.

We could not correlate a six- or 24-hour retention with symptoms. It is argued that the retention of food and secretions, should cause an inflammation of the diverticulum. It seems to us that if this is so, the diverticulum should show tenderness. In other words, if there is an inflammatory reaction, from whatever cause, the diverticulum should be tender to pressure. We have found this tenderness in only four cases and in none of these were the symptoms referable to the diverticulum. We included them in that group because of tenderness, not because the symptoms could be referred to the diverticulum.

We had only 14 cases which were autopsied. Horton and Mueller, from the Mayo Clinic, studied 212 duodenal diverticula found at autopsy, and in none of these were inflammatory reactions noted in the diverticulum.

RAYMOND G. TAYLOR, M.D. (Los Angeles, Calif.): With your indulgence, I will answer the doctor's question about diverticulum of the appendix.

We have the report of one case in our files. The diverticulum was about an inch in diameter, close to the base. It was removed by surgical procedure, so we are sure what it was. I think they are rare.

AN ANATOMIC-ROENTGENOGRAPHIC STUDY OF THE PLEURAL DOMES AND PULMONARY APICES[1]

WITH SPECIAL REFERENCE TO APICAL SUBPLEURAL SCARS

By H. W. JAMISON, M.D., Resident Physician, Department of Roentgenology, Los Angeles County Hospital, *Los Angeles, California*

THIS study is undertaken with the purpose of investigating certain normal shadows seen commonly at the apices of the lung on roentgenograms of the healthy chest. Of little significance in themselves, they derive considerable importance from the fact that they may be misinterpreted as representing disease of the lungs or pleura, particularly apical pulmonary tuberculosis. It is believed that accurate evaluation of apical shadows requires not only precise anatomic knowledge of the pleural domes and pulmonary apices, but also familiarity with certain simple concepts of the mechanism of shadow production by which normal structures may cast visible shadows on the roentgenogram.

Apical parenchymal disease is briefly discussed, mainly for the purpose of contrasting normal with abnormal apical linear shadows. Special reference is made to apical subpleural scars.

ANATOMY

The pleural dome by strict anatomic definition is that portion of the parietal pleura covering the summit of the lung and situated above the superior orifice of each thoracic cage. The plane of this orifice corresponds to the upper surface of the first rib and forms an angle of 45 degrees with the horizontal. In exposing the pleural dome, the various structures encountered may be considered in the nature of a series of enveloping sheaths, as follows: (1) skin and subcutaneous tissues; (2) an outer muscular layer; (3) an inner muscular layer; (4) a fibrous sheath; (5) a vasculo-nervous sheath; (6) the parietal pleura.

Roentgenographically, the "apical region" is ordinarily understood to designate that portion of the chest situated above the level of the clavicle, as seen on the flat postero-anterior film. This region includes, in addition to the above named structures, the posterior and lateral portions of the upper three or four ribs, the associated intercostal soft tissues, and the upper mediastinum.

Skin and Subcutaneous Tissues.—The thickness and tonus of the subcutaneous tissues is a direct expression of the subject's age, habitus, and state of nutrition and is of importance in determining the relative radiolucency of the apices on the film. The thin broad platysma muscle, located anteriorly, is included as an essentially cutaneous structure.

External Muscle Group.—The sternomastoid muscle arises by a sternal head from the anterior surface of the manubrium and by a clavicular head from the sternal third of the clavicle. It covers the anterior aspect of the apex more or less completely.

Postero-lateral to the apices are the levator scapulæ muscles (above) and the serratus anterior muscles (below), while directly posterior, associated with the upper thoracic spine, are the heavy erector spinæ muscles (splenius, semispinalis, etc.), as well as the rhomboids and trapezii.

Internal Muscular Group.—Posterior and lateral to the apices are the three scalene muscles forming a box-like compartment about the pleural dome. The insertion of the anterior scalenus is on the scalene tubercle of the first rib where it separates the subclavian vein and artery. The anterior scalenus insertion is constantly

[1] Written in fulfillment of a requirement of the Residency in Roentgenology, Los Angeles County Hospital.

prolonged over the antero-lateral aspect of the dome, playing an important rôle in the suspension of the pleura.

The Fibrous Sheath.—Between the parietal pleura below and the scaleni above, the structures in relation to the pleural dome are enclosed in loose connective tissue which condenses into a denser layer where it joins the pleura. Supporting this fibrous dome is a series of suspensory ligaments, well described by Cordier and Devos, as follows:

"The pleural dome is maintained in place by an ensemble of fibrous fasciæ and muscles, as described by Zuckerkault and Sebileau under the name of 'suspensory apparatus of the pleura.'

"1. Transpleural ligaments or muscles: The most constant arises from the anterior tubercle of the transverse process of C-7; its inferior insertion extends along the anterior slope of the pleural dome. Partly fibrous, partly muscular, it is attached by a fibrous fasciculus to the first rib near the tubercle of Lisfranc.

"2. The costopleural ligament: It arises from the first rib two or three centimeters from its vertebral extremity; its insertion is in the pleura of the posterior slope of the cupola, enclosing the first dorsal nerve root.

"3. The vertebro-pleural ligament: This is a little inconstant fibrous band arising from the bodies of C-6 and C-7 and ending in the medial slope of the dome."

The Vasculo-nervous Sheath.—Surrounded by connective tissue of the fibrous sheath and separated by it from the parietal pleura are certain blood vessels and nerves which course over the pleural dome in a veritable vasculo-nervous cupola. The anterior slope is primarily a vascular slope in relation with two great vessels: (1) The subclavian vein crosses the pleural dome near its base anteriorly at the level of the clavicle. (2) The subclavian artery describes a curve in intimate relation with the mid-portion of the pleural dome and produces a distinct indentation of the latter, more marked on the left. Three of the artery's main branches are in close association with the pleural dome—an internal mammary, directed anteriorly, a cervico-intercostal, directed posteriorly, and a subscapular, directed laterally. The posterior slope is primarily a nervous slope in relation with the stellate ganglion and with the lower roots of the brachial plexus (C-8 and T-1) as well as the supreme intercostal artery.

The Parietal Pleura.—The configuration of the parietal pleura is described by Cordier and Devos as follows:

"As to its form, the pleural cupola does not describe a uniform curve. Its anterior slope is longer. Its posterior slope is shorter and more abrupt. The highest point of the dome is not exactly in the mid-line but is closer to the neck of the first rib than its sternal extremity. This point projects one to two centimeters above the sterno-clavicular articulation and two to three centimeters above the sternal extremity of the first rib."

The Posterior Thoracic Wall of the Roentgenographic Apex.—The first rib is so oriented that its internal border is located at practically the same level as the external border. For this reason the internal border, to which is attached the pleural dome, causes a slight imprint on the dorsal and lateral surface of the anatomic summit. The second rib describes a much wider arc than the first. The soft tissues connecting these two ribs form an oblique band varying from 25 to 40° from the vertical. The intercostal band between ribs two and three is oriented a little less obliquely, and lower intercostal bands are directed more and more nearly vertically. The soft tissues comprise the internal and external intercostal muscles, the intercostal nerves and blood vessels, and subpleural adipose and connective tissue.

The Interapical Mediastinum.—The soft tissues of the upper mediastinum together with the spine form a broad partition between the apices. On cross-section this partition presents an hourglass appearance, the anterior half of which is formed by the soft tissues, the posterior by the spine and transverse processes. The soft tissues include, from behind forward, the esophagus, trachea, nerves, great blood vessels, thyroid gland (lower pole ordinarily at the level of the apical summit), and the subhyoid muscle group. In association with the antero-lateral aspect of

the spine are the longus colli muscles. The mediastinum widens from below upward, the result of lateral divergence of the internal jugular veins and common carotid arteries, together with associated fascia and areolar tissue. This divergence is such that each internal jugular vein, in

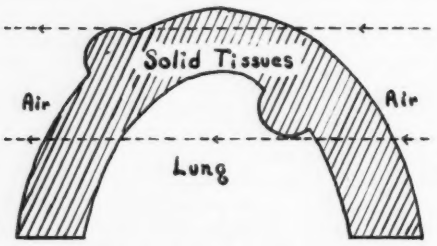

Fig. 1. Mechanism of production of apical linear shadows. (Roentgen rays projected tangentially to surface prominences produce sharply defined linear markings.)

relation with the antero-medial aspect of the corresponding apex at its base, comes to lie directly anterior to the mid-point of the apex at its summit.

The Lung Apices.—The lung apices present the following special features:

1. They completely occupy the apical cupolæ and show impressions corresponding to those of the pleural dome.

2. The apical bronchus on each side arises from the main upper lobe bronchus as the most medial of its three large branches. It is a large trunk measuring nine millimeters (external diameter) at its origin, and is directed vertically upward. It bifurcates in the subapical region into two principal trunks, a small anterior trunk and a posterior apical trunk twice the size of the preceding. The latter ventilates the upper lobe above the level of the first rib (Coulouma). Birch-Hirschfeld has called attention to the peculiar shape of the apical bronchi—they have the appearance of being stunted.

3. The artery is applied to the medial aspect of the apical bronchus closely following its ramifications. Although not so closely applied to the bronchus as the artery, the vein drains an exactly similar area.

4. Rouvière has described in the upper lobe three lymphatic zones including a superior where vessels arising in part from the apical region of the lung (both from the subpleural plexus and paravascular lymphatics) drain to paratracheal glands.

5. Occasionally an accessory azygous lobe is present at the right apex formed as an embryonic developmental anomaly, the result of failure of the azygous vein to shift from its fetal position over the apical cupola to the normal mediastinal location, the vein, instead, drawing down a double fold of parietal pleura as it takes a more direct course to the right lung root.

6. It has been repeatedly shown that the rate of circulation of blood and particularly of lymph in the lungs is markedly dependent upon respiratory movement (Brock and Blair, Drinker and others). Since respiratory excursions of the apices are relatively limited as compared with other portions of the lung, it follows that the respiratory acceleration of blood and lymph flow must also be relatively diminished at the apices. The apices are less mobile because of the narrowness of this portion of the pleural cavity, and because they are so far removed from the diaphragm that they are relatively little affected by its respiratory excursions (O. H. Brown). Hart believes that the slanting first rib girdles compress the lung apices, interfere with their ventilation, and embarrass the blood and lymph flow. Pottenger says that the lung of the child grows out of proportion to the growth of the chest and that this disproportion is especially noticeable in the upper thorax. As a result the lungs undergo compression, relatively more marked at the apices, as the child grows to adulthood, leading to narrowing of the lymph spaces and air cells and retardation of blood and lymph flow.

APICAL ROENTGEN SHADOWS

An apical structure produces a visible linear shadow on the film only (1) when placed in juxtaposition to another structure of strikingly lessened radiographic density, and (2) when so oriented that it

presents a distinct surface or marginal prominence, which the roentgen rays may strike tangentially. Practically speaking, apical structures produce visible linear shadows only when seen as distinct projections either at the endothoracic or skin surface in contrasting relationship with air or air-filled lung. Roentgen rays projected tangentially to the surfaces of such prominences produce sharply defined linear contours (Fig. 1). Structures which produce no surface saliences add to the general density but cannot be seen on the films as separate and distinct entities.

The Supraclavicular Border Shadow.—This is a linear shadow two to five millimeters wide in relation to the upper border of the clavicle, representing skin together with a thin layer of subcutaneous connective tissue as it crosses the prominence of the clavicle. It is ordinarily visible as far medially as the clavicular attachment of the sterno-mastoid muscle.

The Sterno-mastoid Muscle Shadow.—A sharply defined vertical linear shadow crossing the lateral half of the apex marks the lateral margin of the sterno-mastoid. It can be traced upward into the neck well above the upper limits of the apex. It terminates at the clavicle inferiorly, often appearing to fuse with the supraclavicular border shadow. It tends to be more prominent in persons of slender habitus and in the aged, *i. e.*, in those persons in whom the sterno-mastoid can be seen as a distinctly visible surface prominence; conversely, in persons of obese habitus it is seen as an indistinct shadow, if at all.

Mediastinal Shadow.—The structures of the upper mediastinum fuse into a homogeneous density, the individual components of which are indistinguishable except for the trachea, which is visible by reason of air contrast. The left lateral mediastinal border ordinarily appears sharply delimited by a linear shadow representing the lateral border of the subclavian artery. The right lateral mediastinal border is less clearly demarcated, gradually fading off into radiolucency of air-filled lung tissue.

The haziness and lack of detail commonly observed at the medial halves of the apices may in part be attributed to overlying vascular shadows. By injection of the great vessels with opaque substances postmortem we have shown that the internal jugular veins and common carotid arteries cover the medial halves of the apices at their summits, converging below. The lateral border of each internal jugular vein was shown by such methods to correspond on the film approximately to the point of intersection of the internal margins of the first and second ribs.

The shadow of the sterno-mastoid muscle is a further contributory factor to the medial apical haze. The added density of this structure tends to obscure lung detail when the film is relatively underexposed, but may actually accentuate the bronchovascular reticulum on relatively overexposed films.

The Border Shadow of the First Rib.—This shadow is seen as a faint but sharply defined homogeneous density applied to the medial border of the first rib in its posterior third. It varies from 2 to 5 mm. in width (more often than not approaching the latter figure) and measures from 1.5 to 2.5 cm. in length. It is wider behind, tapering anteriorly and disappearing approximately at the point where the first rib begins to recurve toward the midline.

Zawadowski offers the following explanation for this shadow:

> "The first rib takes a very oblique course such that its internal border in its upper portion is at the same level as its external border. This results in the medial border of the first rib becoming countersunk into the lateral surface of the lung apex, the latter rising above it. The boundary between air-filled parenchyma and solid tissue describes at this point a little curve (*courbe*) which touched tangentially by the rays produces a linear shadow having the density of soft tissues and paralleling the medial border of the rib." (See Fig. 1.)

Knuttsen (quoted by Pendergrass) and Andrus, on the other hand, attribute this shadow to direct visualization of a connective-tissue fascial band corresponding

to the fascia of Sibson (Sebileau) previously described.

The Border Shadow of the Second Rib.—This shadow is narrower (1 to 3 mm.) than the border shadow of the first rib but considerably longer. It is usually bilaterally symmetrical. The clean-cut lower margin of the shadow forms an arc exactly paralleling the lower border of the second rib in its postero-lateral one-third to one-half, that is beyond the point where the first rib appears to cross it on the film, and often as far as the point where the second rib begins to recurve toward the midline. Albers-Schönberg, Assmann and others considered this shadow to represent the upper limit of the lung. It has been shown, however, that the shadow persists unchanged after pneumothorax. Zawadowski believes that the shadow is best explained by the fact that anatomically the internal surface of the parietal pleura does not show a regular curve but presents small projections adjacent to and paralleling the lower borders of the ribs. Such projections are produced mainly by subpleural adipose tissue which is not uniformly distributed but tends to accumulate at the lower rib margins. A contributing factor is the presence at the lower rib margins of the intercostal blood vessels. The arteries

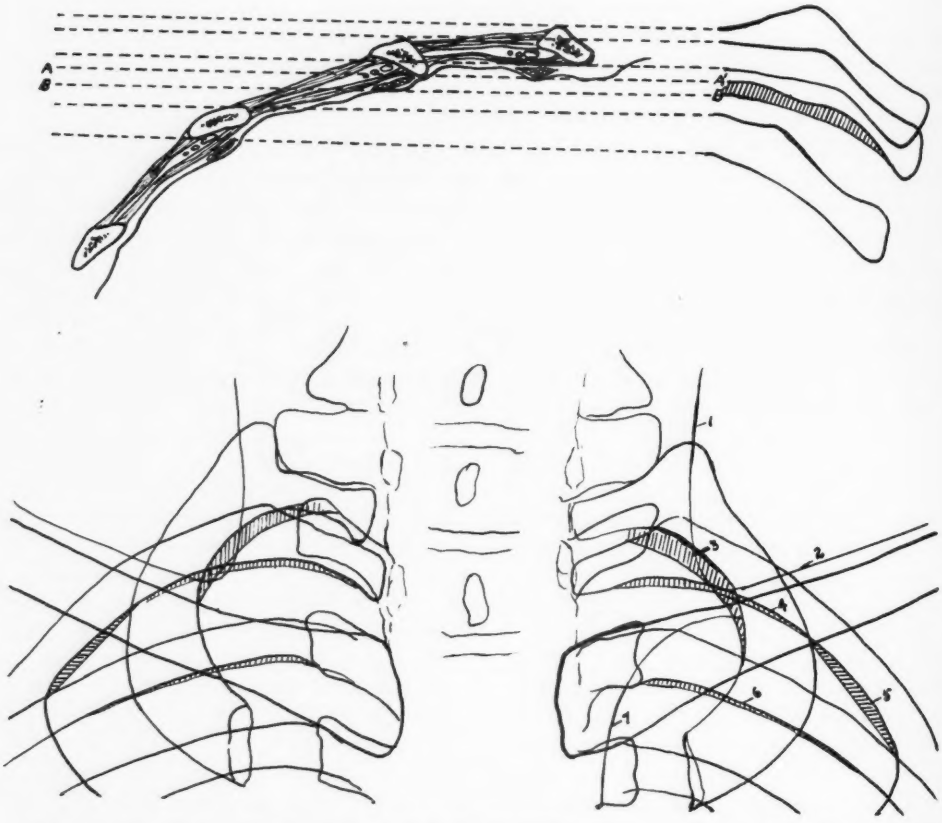

Fig. 2 (*above*). Mechanism of production of the border shadow of the second rib. (*After Zawadowski.*)
Fig. 3 (*below*). Apical linear shadows: a composite diagram. 1, Sterno-mastoid shadow; 2, Supraclavicular border shadow; 3, Border shadow of the first rib; 4, Border shadow of the second rib; 5, First intercostal shadow; 6, Border shadow of the third rib; 7, Left subclavian artery shadow.

are not important in this regard (with the notable exception of coarctation of the aorta). The veins, on the contrary, dilate on expiration and thus elevate the pleura. A further factor is the elastic tension of external tissues on the intercostal bands which results in a slight countersinking of the ribs, thus accentuating the small submarginal prominences.

same manner. Border shadows of lower ribs are not seen by reason of the fact that the intercostal bands are too nearly vertical to satisfy the physical conditions stated above. Knuttsen believes that the "companion shadow of the second rib" is produced by visualization of subcostal muscles which, he states, are found as far medially as the angle of the second rib.

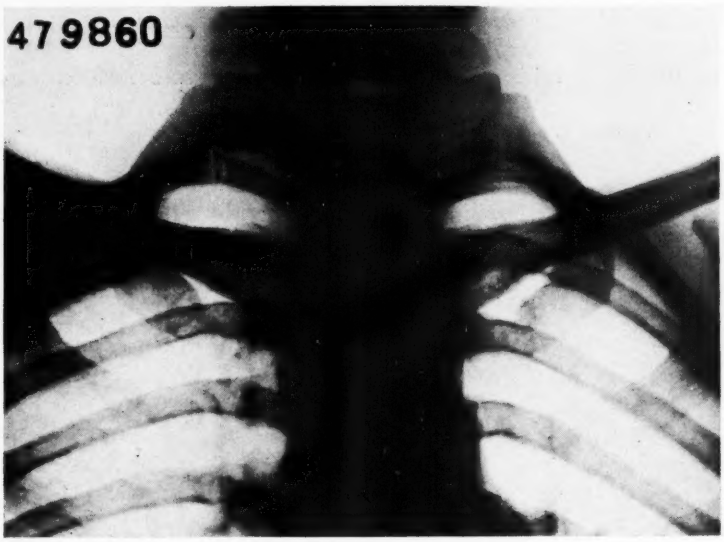

Fig. 4. Pulmonary apices. Note supraclavicular border shadows, border shadows of the first ribs, first intercostal shadows, and left subclavian artery shadow.

Now the dorsal surface of the upper portion of the thorax is not directed in a plane parallel to the long axis of the body but forms a markedly accentuated arc with dorsal convexity. When inclining the trunk slightly forward in the position customarily assumed for chest radiography (with the aim of bringing the anterior surface of the chest as close as possible to the film), the dorsal surface of the upper thorax is brought to an almost horizontal position. The small prominences at the lower borders of the second ribs are thus placed in such a position as to be brought out in profile so that the rays striking them tangentially will produce visible shadows on the film. (See Figs. 1 and 2.)

The occasionally visible border shadow of the third rib is produced in exactly the

Mesial to this point, he believes, the shadow is produced by connective tissue.

A second type of border shadow of the second rib, entirely different from that described above, is seen stereoscopically to lie well anterior, appearing to extend between the first and second ribs laterally, evidently corresponding to the soft tissues of the first interspace.

In speaking of border shadows, it is necessary to mention the bony flanges commonly seen at the lower margins of middle and lower ribs. These are not infrequently seen at the lower borders of the third rib but rarely at the lower borders of ribs one and two. They are readily distinguished by their undulating marginal outlines and, when present, by a characteristic bony spongiosa pattern.

Apical Vascular Shadows.—Of numerous blood vessels which we have described as being more or less intimately related to the pleural dome, only one is seen on the film with any degree of regularity, namely, the left subclavian artery. The explanation becomes apparent when one examines the endothoracic aspect of the pleural dome after removal of the lungs at autopsy. It will then be seen that only the left subclavian artery and right subclavian vein (and occasionally the internal mammary arteries) are visible as projections on the great majority of chest films either in whole or in part. More often than not, only the mediastinal portion or a small medial apical portion of the artery is seen.

The incidence of the various normal apical roentgenographic shadows we have described is indicated in Table I. The findings are based on a study of 200 unselected chest roentgenograms of patients of varying ages (over 15) and of both sexes.

Apical Parenchymal Shadows.—The old

TABLE I.—INCIDENCE OF APICAL LINEAR SHADOWS

Linear Shadow	Percentage Visible	Unilateral	Bilateral	Remarks
Sterno-mastoid shadow	50	7	43	12 per cent seen lateral to apices
Supraclavicular border shadow	68	3	65	
Border shadow of first rib	42	16	26	When unilateral, more commonly seen on right
Border shadow of second rib	46	10	36	
Border shadow of third rib	2	0	2	Marginal bony flange seen in additional 23 per cent
First intercostal shadow	33	12	21	
Subclavian artery shadow	74	72 (all left-sided)	2	26 per cent mediastinal only; 27 per cent extending across half or less of apex; 21 per cent across more than half of apex

endothoracic surface. The same mechanism of shadow production applies to visualization of this artery as previously described in relation to the border shadows of the first and second ribs (Fig. 1). The right subclavian vein, located as it is posterior to the sternal end of the clavicle, would hardly be expected to produce a visible shadow through the greater opacity of the clavicle.

The left subclavian artery shadow is seen as a faintly defined homogeneous density fading above but limited below by a clean-cut linear marginal shadow which describes a semicircular arc across the apex beginning at the mediastinum and ending at the medial border of the first rib. The uppermost portion of this arc is commonly at the level of the lower border of the third posterior rib but varies about one centimeter either above or below this level. This arc shows a vertical medial continuation as far as the aortic arch representing the mediastinal portion of the artery. The artery is visualized in the

dictum that bronchovascular shadows visualized above the clavicular level indicate pathology has long been abandoned as films of fine technical quality have been developed. Indeed, it has become the rule rather than the exception to see such shadows on the routine chest film. These shadows tend to accentuate with advancing age, but all show a common feature, namely, that as they extend toward the lung periphery, they gradually and persistently narrow, fading off into nothingness as the lung surface is approached. Any peripheral thickening of the bronchovascular reticulum at the apices at once arouses suspicion of tuberculosis. We have learned to our discomfiture, however, that certain of these peripheral thickenings may actually represent pathology other than tuberculosis. An occasional apical bronchiectasis is encountered. Small apical bullæ may produce linear shadows simulating tuberculosis as well as appearances resembling cavities. (Absence of circumadjacent parenchymal infiltration will or-

dinarily render the diagnosis apparent in these cases.) Pneumonic infiltration in the late resolution stage may produce thickening of the bronchovascular pattern simulating an exudative tuberculosis. In these cases the history is of decisive importance. Occasionally bronchogenic carcinoma, suppurative pneumonitis, coccidioides, or an apical infarct will require differentiation.

Multiple linear or patchy shadows at the apices, however, will in the vast majority of cases prove to be tuberculous in origin. The presence of these shadows does not necessarily indicate a lesion of serious import. The marked frequency of small nodular or linear fibrotic lesions at the apices with or without enclosed small caseous or calcific centers has been repeatedly noted at autopsy, often with no clinical history of tuberculosis or of a tuberculosis-like episode. Such lesions are frequently discovered accidentally on routine chest films. Assmann, Rediker, Opie, Douglas, Pinner, and others have called attention to the relatively benign character of primary apical (hematogenous) tuberculosis.

A single right apical linear shadow is occasionally encountered representing the pleural fissure demarcating the accessory azygous lobe from the upper lobe. It is seen to extend obliquely downward and medially in the right apical and subapical region ending in a small round density, the azygous vein.

Apical Subpleural Scars.—Certain other shadows of a different nature are frequently encountered at the extreme lung apices and commonly designated as apical pleural caps, apical pleural thickening, or apical pleural scars. These lesions have been a source of considerable discussion both as to etiology and prognostic significance. The question has been raised as to whether all these scars are in fact the result of tuberculous infection, or whether non-specific indurative processes may lead to similar changes. Most authors, including Aschoff, Loeschke, Jaffé, Fishberg, and Calmette, believe they are all uniformly tuberculous in origin, while Scheuermann,

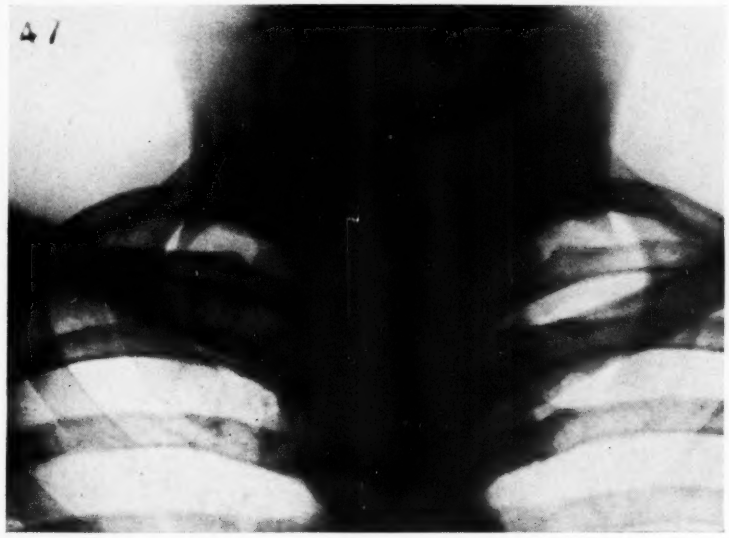

Fig. 5. Pulmonary apices. Note sternomastoid shadows, supraclavicular border shadows, border shadows of the first ribs, border shadow of the right second rib, and left subclavian artery shadow.

Lubarsch, and others believe that one is not justified in calling every apical scar tuberculous.

Fishberg, Sergent, German, and Calmette have described a primary apical pleurisy as an abortive form of apical tuberculosis. Fishberg writes:

"Pleura covering the apex of the lung is almost invariably implicated in tuberculous lesions of the upper lobe of the lung. But at times the pleural lesion is, in the clinical sense, primary, and its symptoms precede those of the pulmonary lesion, or it is not at all followed by a parenchymatous process. . . .

"The onset is insidious. The patient is troubled with mild fever, unproductive cough, pain in the chest or shoulder coupled with anorexia. . . .

"Apical pleurisy is apt to recur. In some patients under my care there have been several relapses at irregular intervals until finally the symptoms of apical pleurisy merged with those of apical pulmonary tuberculosis, the process invaded the parenchyma, and symptoms and signs of an apical lesion could be made out."

Van Zwaluwenburg and Grabfield have felt that the cervical nodes and lymphatics form a direct path by which tubercle bacilli may reach the apex from the tonsils and adenoid tissues of the pharynx. According to their studies cases with tuberculous deposits in the faucial tonsils showed an apical pleuritis in 93 per cent, while cases without tuberculosis of the tonsils showed an apical pleuritis in only 11 per cent of cases. They stated that the more sharply defined, denser type of pleural cap was quiescent, whereas the less dense caps, showing an irregular visceral surface, indicated a process not yet fully cicatrized and capable of progressing along the connective-tissue elements of the parenchyma, and in certain cases, of developing into clinically active pulmonary tuberculosis. They believed, however, that as a rule the pleura formed a very effective barrier to the further progress of the disease.

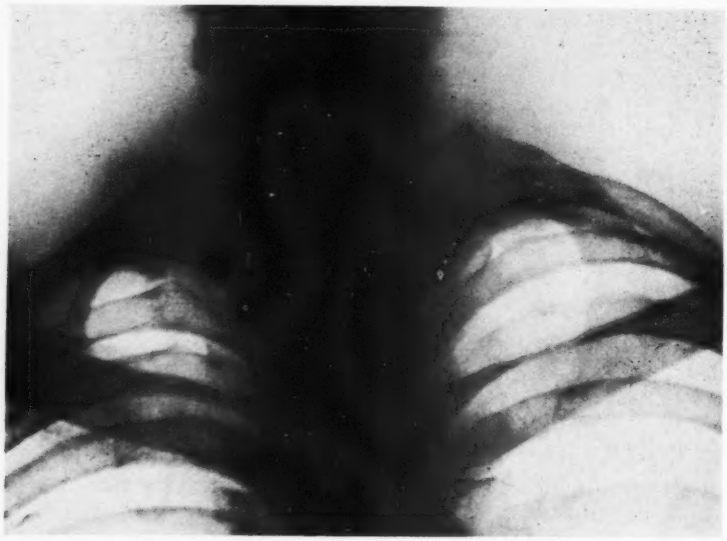

Fig. 6. Pulmonary apices. Note bilateral apical subpleural scars.

Pohle, Paul, and Beatty noticed an incidence of 31 cases of apical pleural thickening in 2,719 routine chest roentgenograms of university students. It was their opinion that in this particular age group the finding of apical pleural thickening was of more significance than in patients of more advanced age.

The problem was thought of sufficient importance to warrant further study. Accordingly, with the co-operation of the

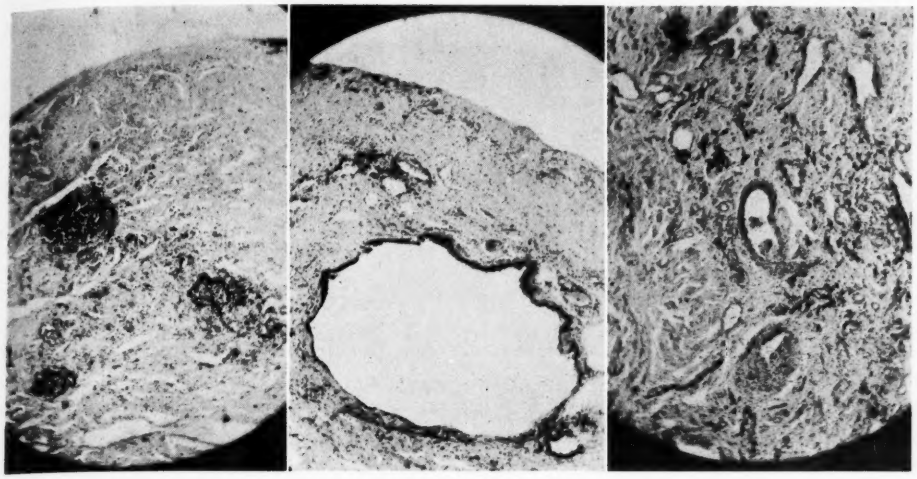

Fig. 7. Fig. 8. Fig. 9.

Fig. 7. Apical subpleural scar. Note hyalinized connective tissue and groups of small lymphocytes.
Fig. 8. Apical subpleural scar. Bronchiectatic dilatation of terminal apical bronchiole.
Fig. 9. Apical subpleural scar. Abundant pigment present.

pathology department of the Los Angeles County Hospital, we collected and preserved for examination the lung apices from 109 consecutive autopsies of nontuberculous individuals 15 years of age or over. The gross and microscopic features of the lesions were noted; their roentgenographic manifestations were studied by reference to chest films taken prior to death, and correlations as to age, sex, and race were made. Of the 109 cases examined, 63 showed apical pleural thickening, an incidence of 57 per cent. In 61 per cent of cases lesions were bilateral; in 22 per cent, right-sided alone, and in 17 per cent, left-sided alone. Grossly, the apical subpleural scar is seen as a 1 to 3 mm. subpleural thickening, usually pigmented (often deeply so), of firm, almost cartilaginous consistency, in the great majority of cases located exactly at the summit of the apex. Only five of the 63 lesions were more than 2 cm. from the summit. Forty-seven per cent were 1 cm. in diameter or less; the remainder varied from 1 to 4 cm. in greatest diameter, the larger lesions usually showing an irregular lobulated or stellate form; the majority were about 1 mm. in thickness. The parietal surface was almost invariably smooth, but the visceral surface often showed small irregular tent-like projections, more noticeable in the softer, thicker lesions. Of the 109 cases, nine showed local apical adhesions, and of these, five were accompanied by subpleural scars: three of the 63 scars were calcified.

TABLE II.—AGE INCIDENCE: APICAL SUBPLEURAL SCARS

Age	No. Cases	No. with Scars	Percentage with Scars
15–25	9	0	0
26–35	8	2	25.0
36–45	12	6	50.0
46–55	16	10	62.5
56–65	28	19	67.8
66–75	25	16	64.0
Over 75	11	10	91.0
Under 45	29	8	27.6
Over 45	80	55	68.8
Total	109	63	57.7

Ten of the thicker and softer of these lesions were selected for section. None showed microscopic appearances characteristic of tuberculosis such as tubercle formation, giant cells, granulation tissue, or caseation. Only one showed evidence of silicosis by the polarizing microscope, and this in relatively small amount. Most contained varying amounts of pigment.

TABLE III.—AGE INCIDENCE: ROENTGENOGRAPHIC SHADOWS OF APICAL SUBPLEURAL SCARS

Age	No. Cases	Negative		Unilateral Lesion		Bilateral Lesions		Questionable Lesions	
		No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage
15–25	61	57	93.4	2	3.3	0	0.0	2	3.3
26–35	48	43	89.6	2	4.2	1	2.1	2	4.2
36–45	37	25	67.5	1	2.7	6	16.2	5	13.5
46–55	36	22	61.2	2	5.5	7	19.4	5	13.9
56–65	41	20	48.8	6	14.6	8	19.5	7	17.1
66–75	24	9	37.3	3	12.6	8	33.4	4	16.7
75—	6	3	50.0	1	16.7	1	16.7	1	16.7
Under 45	146	125	85.7	5	3.4	7	4.8	9	6.1
Over 45	107	54	50.4	12	11.2	24	22.4	17	15.9
Total	253	179	70.8	17	6.7	31	12.2	26	10.3

The scars were composed for the most part of dense hyalinized connective tissue. Small localized collections of lymphocytes were a common feature. Blood vessels were relatively few and of comparatively large size. Bronchiectatic dilatations of terminal bronchioles were common, probably the result of traction on their walls by contraction of fibrous tissue.

Women numbered 44 of the cases studied; of these, 24 showed subpleural scars, an incidence of 55 per cent. Of the 65 males, 39 (or 60 per cent) showed apical subpleural scars.

All but 16 of the 109 cases were of the Caucasian race. Of eight Mexicans, there were three with pleural scars; average age 48 years. Of seven Ethiopians there were four with pleural scars; average age 37 years. One Mongolian patient, aged 17 years, had no pleural scars. When the incidence of the lesions was correlated with age a very striking fact emerged, namely, a pronounced and progressive increase in frequency with advancing age, as indicated in Table II.

In not over half of the cases in which at autopsy we recognized typical scars could such be identified on review of previous films when available and of satisfactory quality. In a study of 253 additional chest roentgenograms of non-tuberculous persons 15 years or over in age, a surprisingly small percentage showed definite roentgen evidence of pleural scars.

Considering the small size and thinness of a large percentage of the lesions we have described, it is not remarkable that many cast no visible shadow on the film. Many are presumably obscured by the images of the superimposed posterior extremities of the first and second ribs (or first, second, and third). At the medial slope of the apex they would be overshadowed by the soft tissues of the upper mediastinum. Such lesions could hardly be expected to become visibly manifest on the anterior or posterior slopes of the apex in cases in which the increment of their density as compared to that of the enveloping soft tissues would not be sufficient to register on the film as separate and distinct shadows. Only when seen tangentially in favorable position for contrasting relationship with air-filled lung may such lesions be expected to become visible on the film.

The subpleural scar is seen roentgenographically as a 1 to 5 mm. linear shadow usually visible at the lower border of the second posterior rib. It differs from border shadows of the first and second ribs, with which it is most likely to be confused, in the following respects: (1) it lacks homogeneity; (2) it is usually of greater density; (3) it lacks symmetry when bilateral lesions are present; (4) it frequently presents an irregular, tented, or undulating lower border in contrast to the perfectly regular, finely pencilled marginal outline of the normal border shadow; (5) it may appear to cross the shadows of the first and second ribs at any angle; (6) it does not conform to the characteristic pattern of the border shadows of the first and second ribs.

Of 253 unselected chest films of non-tuberculous individuals 15 years of age or over, 48 showed definite apical summit

shadows corresponding to apical subpleural scars. In 26 additional cases the presence of subpleural scars was questionable. Age incidence is noted in Table III. Increasing frequency of these lesions with advancing age is again noted.

DISCUSSION

Lack of microscopic evidence of tuberculosis in those lesions sectioned, together with evidence of increasing frequency closely paralleling advancing age, would tend to indicate that not all these lesions are of tuberculous etiology, and that at least a considerable percentage may well be of non-specific origin.

Graber (quoted from Van Zwaluwenburg) has injected the pharyngeal wall of dogs and guinea pigs with India ink and killed them at varying intervals after injection. He found that particles were carried down the cervical lymph chain to the bronchial nodes and finally to the apical pleura. It would be theoretically possible for bacteria from the oral cavity and pharynx to reach the apical pleura by similar channels. Such bacteria could then set up a local inflammatory process in the subpleural lymphatics, aided by relative stagnation of apical lymph flow, leading to reactive subpleural fibrosis and scarring.

An alternative source of apical subpleural lymphatic infection would, of course, be the lung itself. We have already referred to the relatively large amounts of pigment found in subpleural scars. Deposition of pigment in the lymphatics of the apical subpleural plexus is probably no greater than in other portions of the lung, but because of relative stasis of apical lymph flow, due to factors previously described, there is greater tendency toward accumulation of foreign material in these channels. The same factors would apply also to bacteria of all types. Repeated bacterial assault over many years would be expected to produce cumulative fibrotic changes in the subpleural lymphatics.

SUMMARY

1. The anatomy of the pulmonary apices and pleural domes is described.

2. Roentgenographic shadows seen at the lung apices are analyzed in the light of anatomy.

Special reference is made to subpleural apical scars. Evidence is presented to show: (1) that such lesions increase in frequency progressively with age; (2) that many, if not the majority, of such lesions may well be of non-tuberculous origin.

The incidence of apical subpleural scars in 109 autopsy cases was found to be 27.6 per cent for persons under 45 years of age and 68.8 per cent for persons over 45 years of age. The incidence of shadows corresponding to apical subpleural scars in 253 chest roentgenograms of non-tuberculous individuals was found to be 8.2 per cent for persons under 45 years of age and 33.6 per cent for persons over 45 years of age.

The possible pathogenesis of such lesions is briefly discussed.

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THE MANAGEMENT OF CANCER OF THE BREAST WITH PRE-OPERATIVE AND POST-OPERATIVE IRRADIATION[1]

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IT is estimated that about 15,000 women die annually of mammary cancer in this country, and it is not unreasonable to assume that more than 50,000 women are afflicted with this disease at the present time (Pfahler, 1). Although statistics show that only about 20 per cent of such patients were cured 10 or 15 years ago, present-day records[2] reveal that as many as from 40 to 50 per cent of all cases can be saved.

What are the factors that may account for this evident improvement in the five-year results in the treatment of breast cancer? The radical surgical technic in the treatment of this condition has not materially changed since its inception, in 1894, by Halsted. In fact, the operative results have not noticeably improved in the past 40 years (Hutchison, 2, and Lewis and Rienhoff, 3). Portmann(4) collected the published statistics of 44 well accredited hospitals and clinics and found the mean average of five-year survivals for cancer of the breast treated by surgery alone to be 28 per cent. Patients do not present themselves for treatment much earlier now than in former years, notwithstanding the publicity campaign of the medical profession and, particularly, the American Society for the Control of Cancer. Less than 10 per cent of all patients with breast cancer present themselves for treatment in the early stage (*i.e.*, a small tumor confined to the breast alone, 1). One of the largest medical centers presented statistics which show that from 35 to 50 per cent of breast cancers are inoperable when first seen, and 62 per cent have already recognizable metastases at the time of the first examination (5). Sad to relate, the education of the general physician in the early recognition of this disease leaves much to be desired.

What, then, accounts for this evident improvement in the final outcome of all types of mammary cancer n the past decade? Or, to state the question differently, what may be considered to be the proper management of breast carcinoma?

DIAGNOSIS

It is axiomatic to assume that a correct diagnosis precedes the proper treatment. Although most cases of mammary cancer can be recognized by physical examination, a considerable number are not so easily diagnosed and require a biopsy. To avoid error, we subject all cases suspected of cancer to an immediate biopsy examination. There should be no temporizing with this dangerous condition. Time is the all-important factor in the ultimate outcome. Whether the biopsy is performed by cautery, by needle aspiration, by the Hoffman punch (6), or by the new Silverman (7) biopsy needle (which, in our hands, has proved quite satisfactory), does not matter as long as sufficient material is removed for examination. Without waiting for the report, treatment is immediately begun. In this way, the possible danger of spreading the cancer by taking the biopsy is minimized. Should the report of the specimen show no evidence of cancer, very little is lost. The treatment is interrupted and the proper course followed for the condition described in the report.

CLINICAL TYPES

Inasmuch as therapy depends upon the stage in which the disease is first seen by the physician, it is well to consider the clinical types or "stages" of breast cancer. We are not referring now to the microscopic grading of carcinoma of the mam-

[1] Accepted for publication in April, 1940.

[2] Estimated from the published records of more than 40 well-known hospitals and clinics.

mary gland, but rather to the early, late, or intermediate stages of the lesion which are elicited by physical examination. The following classification (8), which is a modification of Steinthal's (9) clinical groups, is suggested. In Stage 1 (Fig. 1), the tumor is usua ly small (less than 3 cm. in diameter), freely movable, and confined

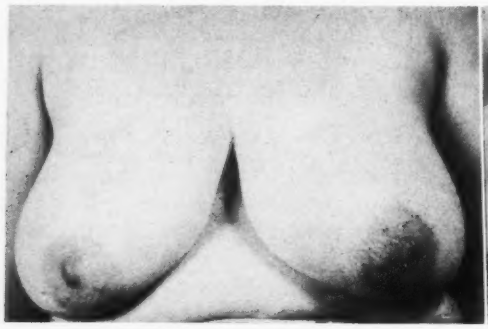


Fig. 1.

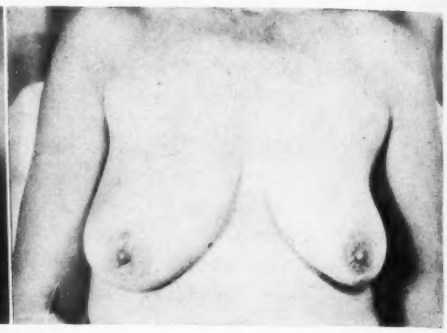


Fig. 2.

Fig. 1. Carcinoma of the right breast in Stage 1. Small, freely movable tumor measuring less than 3 cm. in diameter in the upper outer quadrant. No palpable lymph nodes in the axilla or supraclavicular fossa. The left breast and regional lymph node areas are negative and no distant metastasis is present.

Fig. 2. Carcinoma of the right breast in Stage 2. A mass about 5 cm. in diameter lies above and external to the nipple. The underlying tissues are fairly movable but the skin is less so. A firm hard node is palpable in the right axilla.

strictly to the affected breast. No regional nodes are felt. In Stage 2 (Fig. 2), firm nodes are palpable in the axilla, the primary tumor is usually larger than 3 cm., and partially fixed to the skin and the underlying tissues (pectoral muscle or fascia). When the breast is edematous or its skin has an inflamed appearance, when the tumor is very large (involving a considerable portion of the mammary gland), when it is more or less fixed to the skin and underlying structures, when adherent nodes are palpable in the axilla and in the supraclavicular fossa, or distant metastasis is present, the case is regarded as belonging to Stage 3 (Fig. 3). Recurrent cancer is considered to represent Stage 4 (Fig. 4). It is often necessary to take roentgenograms of the chest or skeletal system before excluding the possibility of the presence of metastases.

MICROSCOPIC GRADING

Microscopically, breast neoplasms are divided into Grades 1, 2, 3, and 4, according to their degree of malignancy (MacCarty, 10). The first grade, showing the more adult type of cell, is the least malignant. The fourth grade, being anaplastic, possesses the most malignant tendency. Grades 2 and 3 show intermediate characteristics between Grades 1 and 4. Because it has been definitely shown that cells of the more adult type (Grades 1 and 2) are less sensitive to the action of the roentgen rays and to radium, whereas the embryonal or anaplastic type of tumor as represented in Grades 3 and 4 is radiosensitive, it was at first believed that the management and even the prognosis of breast cancer could be determined from the grading of the tumor. Experience soon proved that such was not the case (1). First, biopsy specimens representing only one small part of the growth often give a wrong impression of the grade of the entire tumor. By the same token, different sections of the same lesion often show two or even three grades microscopically. Furthermore, seldom do two or more pathologists quite agree upon the

grading of the same tumor, their criteria for each grade often varying considerably. The grade of the metastatic or secondary growth often differs from that of the primary tumor in the breast.

In addition to all these insurmountable difficulties, it was soon discovered that the grading of tumors is not the whole story in considering the treatment and outcome of the case. There is the tumor bed, *i.e.*, the tissues in which the neoplasm is implanted, and there is the patient herself, who, after all, is of primary consideration. Factors in the tumor bed that influence treatment and prognosis are the presence or absence of infection, the blood supply, the resistance of the tissues to tumor spread, the location and size of the neoplasm in the organ, etc. In regard to the patient, age, general nutrition, degree of anemia, complicating medical disorders, etc., are unquestionably significant factors to be considered in planning therapy.

PRE-OPERATIVE ROENTGEN THERAPY

Immediately after the diagnosis of breast cancer is suggested clinically and before the report of the biopsy is received, the patient is given a course of high-voltage roentgen treatments, cross-firing the entire affected breast through two portals. The rays are directed tangentially through the anterior chest wall so that the underlying lung is avoided. Two hundred r (measured in air) are given daily to each of the two portals for a total of from 2,000 to 2,600 r to each area. The following factors are used: 200 kv.p., 50 cm. distance, and 2 mm. copper, 1 mm. aluminum filters. At the completion of the treatments to the breast, the axilla is then cross-fired through anterior and posterior portals. Two hundred r are given daily to each of the two fields for a total of from 1,200 to 1,800 r to each port. The same technical set-up is employed as for the breast. In place of two ports, the axilla may be irradiated directly through one field. The arm is elevated and the rays are directed into the axilla for a total dosage of from 1,200 to 1,400 r. Finally, the supraclavicular fossa is treated, with the technical factors already mentioned, through anterior and posterior ports, each area receiving 200 r daily for a total of from 1,600 to 2,000 r each. With the irradiation already described, the parasternal nodes and the mediastinum receive no small amount of treatment, particularly from the medial breast port and from both supraclavicular areas. The rays through the latter fields are directed slightly toward the mediastinum (Fig. 5). If an intra-axillary area is employed, the direction of the beam is through the axilla and upper mediastinum. As pointed out by

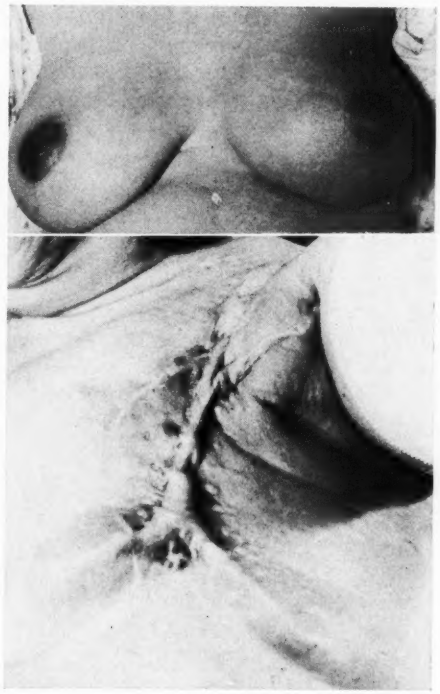


Fig. 3 (*above*). Carcinoma of the left breast in Stage 3. A large, indefinitely outlined tumor occupies a considerable portion of the left breast. The overlying skin is edematous and adherent to this mass, which is partially attached to the pectoral muscle and fascia. The axilla shows evidence of several palpable nodes ranging in size from that of an almond to a pea.

Fig. 4 (*below*). Recurrent mammary cancer. Six months after mastectomy, many skin nodules and several larger subcutaneous masses developed at the operation site. The scar shows keloidal changes.

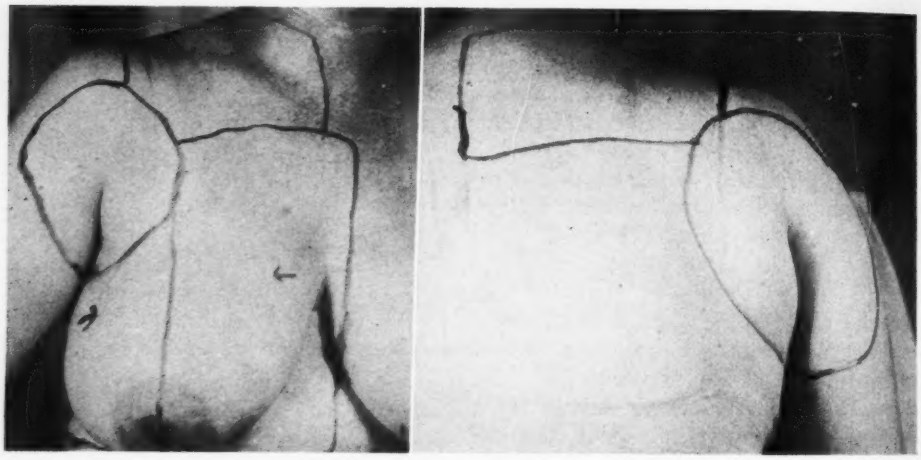
Handley (11), the parasternal nodes along the course of the internal mammary artery frequently serve as a portal of entry for the invasion of the thorax.

This course of treatments is a modified form of Coutard's technic, employing protracted, fractionated, highly filtered rays. Shortly after (and sometimes before) the completion of the treatments for each portal, a pronounced erythema of the skin may develop which goes on to blistering or bullæ formation when the higher limits of dosage are given. Slight desquamation develops or almost complete denudation of the epidermis (Fig. 6-*A*) ensues, depending on the total dosage administered to the field and on the sensitivity of the patient's skin. Occasionally, treatments must be postponed several days or a week during the course because of the skin reaction. The skin must be closely inspected before each séance. However, the skin recovers completely, inasmuch as the treatments have not affected the corium but only the epidermis which grows in nicely without scarring or other permanent changes.

Using the above technic, we have experienced very little radiation sickness.

The above roentgen treatments are completed in from 27 to 33 days. In about two or three weeks after therapy, the height of the epidermolysis has been reached and recovery sets in. Recovery of the skin (Fig. 6-*B*) is truly remarkable, so that in from six to eight weeks it has practically been restored to its former healthy state except for a slightly brownish pigmentation. At this time (about eight weeks after the last treatment) the patient is subjected to a radical mastectomy.

Pre-operative irradiation is given to all patients with cancer of the breast (Stages 1, 2, 3). In most patients a marked diminution in the size of the primary tumor is clinically noted following therapy, and, not infrequently, the mass entirely disappears. The secondary deposits are similarly affected but often to a lesser degree. In 200 cases of breast carcinoma which were subjected to pre-operative irradiation, Adair (12) reported that the surgical specimens as examined by Dr. Ewing and Dr. Stewart showed a total destruction of the primary tumor in 33 per cent and in the axilla in 22 per cent of the cases. We have never seen the tumor mass increase in size during therapy. Cases



A *B*

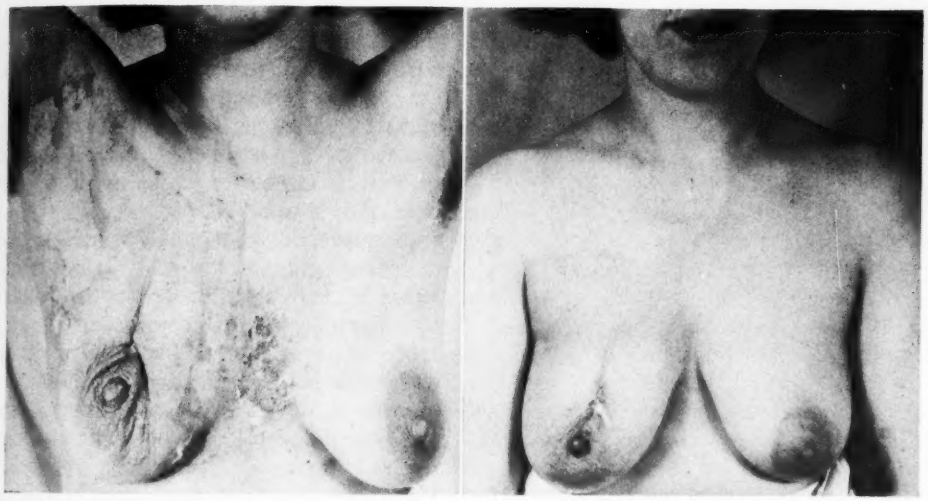
Figs. 5-*A* and 5-*B*. Mammary carcinoma showing the portals of entry for preoperative irradiation. *A*, The anterior fields. Arrows indicate the direction of the central beam. *B*, The posterior ports.

classified in Stage 1 (small, freely movable breast tumor with no palpable nodes) may or may not receive treatments to the supraclavicular fossa but the breast and axilla are always irradiated. The rationale for the treatment given to the axilla is twofold: first, to destroy or inhibit the growth of any possible malignant cells that may be present and yet are not palpable, and second, to prevent, if possible, subsequent extension to the area. As regards the first possibility, it is a not uncommon experience to find axillary involvement (Stage 2) at operation, whereas previously no nodes were palpable (Stage 1). In other words, a case diagnosed clinically in Stage 1 turns out to be actually in Stage 2 at the operating table.

As regards the second possibility, namely, the prevention by irradiation of subsequent extension of the malignant process, it has been shown by Russ and Scott (13), in their experimental work on rats, that implanted sarcoma and carcinoma show pronounced preference in their growth for unirradiated tissues, avoiding the regions that have been exposed previously to the rays.

Therefore, we feel that all cases should be irradiated pre-operatively. It has been observed not infrequently that an inoperable case has been made operable following this intensive course of therapy. Although patients in Stage 3 have seldom been cured (about 5 to 10 per cent alive and well at the end of five years), irradiation has definitely prolonged life, relieved pain, and changed an intolerable existence into a relatively comfortable one. It is in patients in Stage 2 that the results of irradiation, added to the usual operation, have been most gratifying. With operation alone, only 28 per cent have survived five years with no evidence of disease: irradiation plus operation has increased the percentage of five-year cures to 57. In competent hands there has been no appreciable increased difficulty in performing the operation in cases that have received adequate irradiation (Adair, 14, Cohn, 15, and Leavitt, 16).

Another objection often raised to preoperative irradiation is that surgery is delayed from six to eight weeks during which time the cancer may spread. As mentioned above, it has not been our expe-



A *B*

Figs. 6-*A* and 6-*B*. *A*, Photograph showing denudation of the skin (epidermolysis) following a course of preoperative irradiation. *B*, Same patient four weeks later, showing complete recovery of the epidermis.

rience or that of others to observe any growth of the tumor or nodes during irradiation; in fact, an appreciable diminution in size of the primary mass is the rule, and, occasionally, almost a complete disappearance of the tumor is noted after irradiation (12). The destruction or devitalization of the cancer cells, the sealing off of the lymphatics, the reduction of the blood supply to the tumor (endarteritis), and the increase of fibrosis are some of the effects of irradiation. It is during the six- to eight-week period following therapy that these full effects can be expected. These advantages should not be offset by resorting to surgery too early after the completion of the treatments or by foregoing the distinct benefit of pre-operative irradiation.

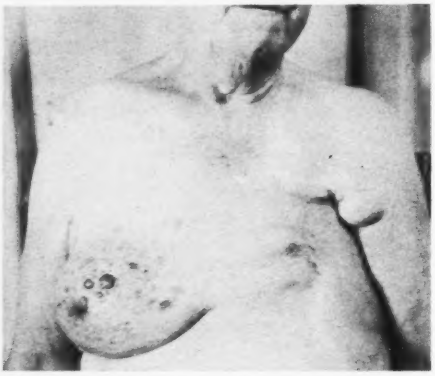


Fig. 7. Numerous large and small skin metastases to right breast one and a half years following radical mastectomy for carcinoma of the left breast.

POST-OPERATIVE IRRADIATION

In from four to six weeks following operation, another series of high-voltage treatments is given. This course is similar to the pre-operative treatments, except that dosage is kept within the lower limits. The anterior chest wall is treated by tangential, obliquely directed rays. Here, again, the skin reaction must be closely watched during the course of therapy. The entire scar is included in the fields of irradiation because of the well-known frequency of stitch-hole recurrence and because of the possibility that cancer cells have been disseminated inadvertently at operation in the skin flaps and underlying tissues. If for any reason pre-operative irradiation was omitted, post-operative therapy is given about two weeks after surgery, or as early as is commensurate with the patient's condition. It is unnecessary to delay treatments until the wound heals completely. Our experience (also that of Pfahler and Vastine, 17, and others) shows that roentgen therapy promotes rather than retards healing of the wound.

The post-operative course of roentgen therapy is indicated to prevent local recurrence and regional metastasis of the growth. As already mentioned, experimental work, as well as clinical experience, has shown that malignant tissue is less apt to gain a foothold or to set up a tumor in previously irradiated areas.

As a rule, only one post-operative course of treatments is given. Further therapy, either by the roentgen rays or by radium, is indicated only in the presence of recurrence or metastasis. The patient is examined semi-monthly for three or four months and then at monthly intervals for the possibility of local or regional recurrences or metastases. The remaining breast and its regional nodes should be included in the examination (Fig. 7). Recurrences are treated as early as discovered, usually by irradiation—x-rays or radium. A large recurrence is apt to be less amenable to therapy than a small or early lesion.

The additional irradiation necessary to treat local and regional recurrences should be cautiously and judiciously applied, bearing in mind that the skin has already been exposed to two episodes of epidermolysis. Nevertheless, such treatments are not contra-indicated. The work of Borak (18) and others on skin exposed to prolonged, highly filtered, fractionated treatments shows that the epidermis completely recovers after the epidermolytic stage as long as the corium is not injured or destroyed. Additional treatments, judi-

ciously applied to such previously irradiated skin, are justified, whenever necessary, without fear of early or late changes or sequelæ in the tegumen.

OVARIAN STERILIZATION

In the last few years, we have recommended the induction of an artificial menopause by irradiation to all menstruating patients with breast cancer. Sufficient experimental and clinical evidence (19, 20, 21) has been accumulated to indicate that the ovarian hormones stimulate the glandular tissue in the breast. It has been known for a long time that breast cancer in a patient under 40 years of age as well as in the pregnant subject is highly malignant. The menopause has an involuting effect upon the breast and its neoplasms as well as on bone metastases from the mammary gland (22, 23). Since the inhibition of ovarian activity tends to produce a concomitant check on the glandular activity of the breasts, the rationale for ovarian sterilization makes the procedure advisable in all women who are still menstruating.

The clinical experience of Ahlbom (24), Torek (25), and others seems to indicate that all patients should be subjected to ovarian irradiation, those past the menopause as well as the younger subjects. Because of the frequent occurrence of mammary cancer after the menopause, the possibility of the ovaries secreting a carcinogenic agent after the cessation of their menstrual function is considered.

Ovarian sterilization is accomplished by irradiation administered either after the completion of the pre-operative course of treatments to the breast or after the post-operative series. A depth dose (at the ovaries) of from 1,000 to 1,500 r is given through two anterior or lower abdominal ports and two posterior or sacral ports. Each port receives from 500 to 600 r, which may be given on alternate days or by the fractionated method, employing the following technical factors: 200 kv.p., 50 cm. distance, 0.5 mm. copper, 1 mm. aluminum filters.

CLINICAL APPLICATION

In the past two and one-half years, 22 patients with proved carcinoma of the breast have been given treatment as described above. Although our series is too small and the elapsed time factor does not permit statistics of five- and ten-year survival rates, nevertheless, we feel that our plan of therapy for breast carcinoma is rational, adequate, scientific, and in accord with the mass of modern experimental and clinical knowledge and personal experience. We are prompted, therefore, to report procedure and technic, notwithstanding the absence of statistical results, flattering ourselves with the hope that others may take note and repeat the principles and procedures herein stated. It is only in this way that really large series of cases can eventually be evaluated, from which invaluable conclusions may be drawn. The inevitably small or limited number of cases reported by any one clinic or group can lead only to inadequate deductions.

The intensive irradiation with which the cancer cells are bombarded by the pre- and post-operative procedures is justifiable both from the standpoint of the nature of the disease, which brooks no compromise, and from the work of Martin, Quimby, and Pack (26), who have demonstrated that from seven to ten threshold erythema doses are necessary to control cancer of the oral mucous membranes and metastatic cancer of the cervical lymph nodes. Our total dosage is as high as possible, approaching the lethal dose as determined by these workers. Portmann (27) referred to this type of treatment as "radical irradiation" and compares it favorably with radical surgery.

The high voltages which present-day equipment is capable of generating and the Coutard principle of therapy, in which small, daily, highly filtered doses delivered through several ports are used to crossfire a tumor below the surface of the body over a period of several weeks, in place of the formerly employed single, lightly filtered, massive doses, account for the in-

creased depth or tumor dose, which represents the actual radiation reaching the new growth itself. Modern technic, embodying these principles, has materially improved the outlook of the present-day cancer patient.

SUMMARY

In conclusion, it is not the aim of the writer to treat cancer of the breast by any hard, fast rules. As a matter of fact, the technic of radiation therapy is constantly changing, and what may be considered adequate scientific therapy to-day may prove insufficient a few years hence. As in cancer in any part of the body, each patient must be individualized and the most rational course of therapy for each subject in the light of present-day knowledge and experience should be outlined and followed. Nevertheless, when the diagnosis of breast cancer is warranted and the stage of the disease is determined, the patient should receive a thorough course of high-voltage x-ray treatments. We are of the opinion that this series of treatments is all-important, and that no compromise with the administration of a short course or an inadequate series should be tolerated.

In Stages 1 and 2 of breast cancer, radical surgery is indicated from six to eight weeks after irradiation, to be followed up by a second adequate course of roentgen treatments from four to six weeks later. Holfelder (28) reports double the number of five-year cures in patients receiving post-operative therapy as compared with those treated by operation alone. Roentgen sterilization of ovaries, we believe, tends to improve the end-results, and is advisable at least in all patients who are still menstruating.

Patients classified in Stage 3 are mainly a radiologic problem. They should receive as thorough a course of roentgen treatments as their condition permits, remembering that the individual must be treated as well as the disease. This is followed up by conservative surgery or radium therapy as the case indicates. Further roentgen therapy is given as it becomes necessary for the relief of pain and discomfort.

The treatment of recurrent cancer (Stage 4) is usually a radiologic problem requiring radium or x-rays or both.

Radiation therapy is a highly technical field, and only expertly trained specialists should be entrusted with its application in the management and treatment of disease.

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KIDNEY STONES SIMULATING BILIARY CONCRETIONS[1]

A ROENTGENOGRAPHIC STUDY

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THE roentgenologist usually experiences little difficulty in differentiating on a routine plain film of the abdomen between roentgenographic shadows produced by urinary concretions and gallstones. In some cases, additional views postero-anteriorly or laterally are needed, supported, if necessary, by stereoscopic, cholecystographic, or urographic studies to clarify the condition.

In a third group, the routine plain abdominal plate is not only insufficient for differential diagnosis but is actually misleading. Upon reviewing 12 modern textbooks on urology, roentgen diagnosis, and urologic-roentgenologic diagnosis, this possibility was mentioned but once (13). There was also a conspicuous absence of illustrations bearing upon this point. The literature of the last decade, likewise, fails to give this subject the consideration which it unquestionably deserves. Publications (10) can be found quoting cases in which the situation was reversed, namely, biliary concretions being erroneously diagnosed as kidney stones.

The practical considerations involved in these differential diagnostic problems occur mainly on studying survey films of the abdomen, lumbar spine, or urinary tract, when the roentgenologist's attention has not been primarily directed to the kidneys. When observing "typical" shadow configurations as accidental findings, the roentgenologist may commit himself to a definite but incorrect diagnosis. However, in those cases in which renal disease is suspected and the patient is sent primarily for urologic-roentgenologic work-up, such misinterpretations are less likely to occur.

The characteristics of biliary concretions are their location over the area of gall bladder and biliary ducts, their ring-shaped or laminated structure with or without a dense nucleus, and facet formation. In multiple concretions, the stones may be homogeneous but their arrangement is such as to outline the shape of the gall bladder. The purpose of this paper is to present three cases which clearly demonstrate these properties but which were proved to be cases of kidney concretions.

Case 1. A female, aged 36, was admitted to the hospital with a history of vomiting, severe pain in the right lumbar region and loin, and localized tenderness over the right wing of the os sacrum and over the right gluteal region. *There were no typical urinary symptoms.* The temperature curve showed high intermittent fever up to 105°. The leukocyte count was 16,200 and sedimentation rate 100 mm. per hour. *A tentative clinical diagnosis of acute osteomyelitis was made.*

Roentgenographic study showed a unilateral sacralization, with marked asymmetry of the fifth lumbar vertebra and consecutive lateral tilting of the lumbar spine against the os sacrum. A high degree of compensatory scoliosis of the middle lumbar spine was visualized, associated with marked torsion and far advanced chronic hypertrophic arthrosis of the spine. There was no roentgenologic evidence of osteomyelitis which, of course, could not be expected as early as 20 hours after the clinical onset. In the region of the gall bladder, a group of round, dense, almost homogeneous calcifications was noted, arranged in the typical fashion of a gall bladder filled with stones (Fig. 1-*a*). The concretions were of equal size, suggesting "one family of gall-bladder stones."

[1] Accepted for publication in April, 1940.

Additional studies revealed a marked enlargement of the right kidney (Fig. 1-*b*). This led to the correct diagnosis of multiple renal concretions. Retrograde pyelography (Fig. 1-*c*) showed a marked isolated distortion of the right middle calix which was narrowed at its infundibulum, while the minor calix was grossly disfigured and enlarged. The group of concretions was encircled by a small wavy contrast band leaving a clearance around each calculus, suggesting either the presence of material not miscible with the contrast urine, or a complex composition of the stones with a radiolucent layer around the dense nucleus. The upper calix and the kidney pelvis appeared perfectly normal; the lower calix appeared slightly compressed. The ureter was tortuous and atonic, lacked normal peristaltic contractions, and was widened in its pelvic portion.

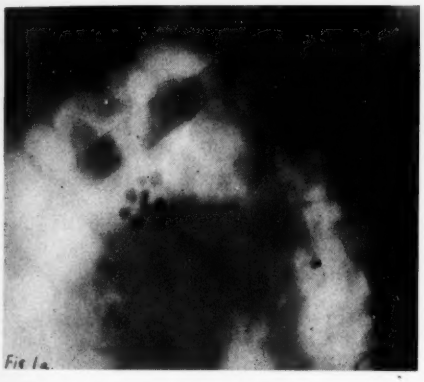


Fig. 1-*a*. Preliminary clinical diagnosis: acute osteomyelitis. The x-ray film reveals multiple concretions which are suggestive of gall-bladder calculi.

Fig. 1-*b*. Case 1. Additional view demonstrates a marked enlargement of the right kidney and a slightly different arrangement of the concretions. Diagnosis doubtful.

Diagnosis.—Enlargement of the right kidney with a group of stones in the mid-calix, possibly due to a markedly narrowed infundibulum which interfered with proper drainage.

Our diagnosis of multiple renal concretions was confirmed two days later when one small stone was expelled with the urine, and subsequently the clinical symptoms subsided. Chemical analysis of the stone revealed earthy phosphates. During the patient's stay at the hospital, seven urine specimens were examined, reaction being acid in five, and alkaline and neutral each in one. Leukocytes were constantly present in moderate numbers, with some epithelial cells, but never any erythrocytes. A smear revealed gram-negative cocci, and on culture *Bacterium coli* was identified.

Summary.—A patient who never presented any urinary symptoms was examined roentgenologically for an acute osteomyelitis. The preliminary flat plate showed a group of calcifications typical in every respect for biliary concretions. Through further x-ray studies these calcifications were identified as multiple kidney stones lodged in one enlarged calix. The subsequent expulsion of a urinary concretion corroborated this diagnosis.

Case 2. A male, aged 27, entered the out-patient department with only one complaint of vague pain over the left side radiating downwards. *No typical urinary symptoms were exhibited.*

Roentgenographic Study.—A preliminary flat plate (Figs. 2-*a* and 2-*b*, *L* to *R* reversed purposely) showed a group of

pathologic calcifications over the left upper abdomen. One shadow, located laterally, was a typical branched renal concretion forming the cast of one calix. In addition, a group of equal sized stones was observed, each stone presenting a typical ring-shaped shell which surrounded a translucent nucleus with a dense center. These stones were so arranged as to simulate the shape of a gall bladder. Two inches higher, one isolated stone was seen, apparently "located at the gall-bladder neck." A

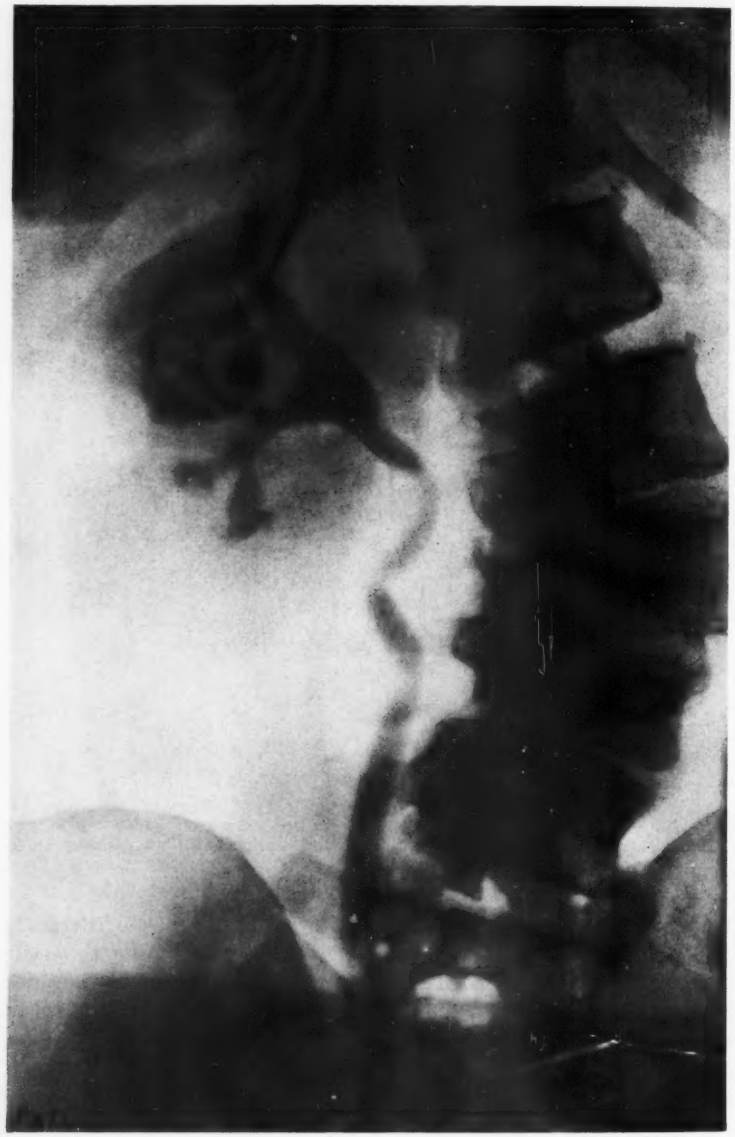
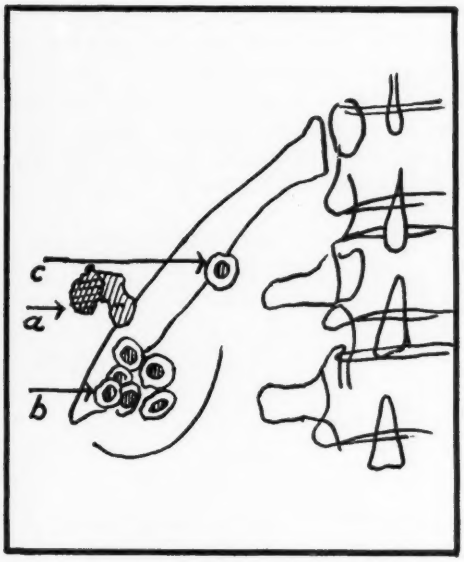


Fig. 1-*c*. Case 1. Retrograde pyelography identifies the concretions as kidney stones lodged in one enlarged minor calix. The infundibulum is narrowed, suggesting poor drainage of the involved calix.

repeat roentgenogram ruled out the presence of a *situs inversus* and possible error in the identification of *L* and *R*. The junction, possibly caused by aberrant vessels and complicated by secondary stone formation on one side.



Figs. 2-*a* and 2-*b*. Case 2 (*R* and *L* reversed purposely). The most likely interpretation would be: (*a*) branched kidney stone, (*b*) multiple concretions within the gall bladder, (*c*) stone at the gall-bladder neck. It was demonstrated (Fig. 2-*c*) that all these shadows represented renal concretions.

fortunate fact that the disease was located on the left side protected us from making the erroneous diagnosis of multiple biliary concretions, with a coincidental kidney stone. Such concurrence of stones within both urinary and biliary systems has repeatedly been reported (3, 6, 19). Excretion urography (Fig. 2-*c*) revealed a considerable enlargement of the left kidney. All the minor calices were greatly widened, forming round outpouchings up to the size of a walnut. The laminated concretions were lodged within the lowermost minor calix, and the branched stone within the minor calix just above the latter. Additional stereoscopic views showed all the concretions distinctly within the confines of the kidney. The kidney pelvis was enlarged, and the ureter was of normal width. On the opposite side, some widening of kidney pelvis and calices was seen, ending abruptly at the pelvi-ureteral junction. From this film we inferred a congenital bilateral narrowing at the pelvi-ureteral

Summary.—A patient who never exhibited typical urinary symptoms was examined for vague unilateral back pain. The plain roentgenogram revealed one branched kidney stone and a group of multiple laminated round concretions which could be used for textbook illustrations of gall-bladder stones. The deception was aggravated by the presence of a similar single stone shadow "over the gall-bladder neck." The location of the pathology on the left side, together with the findings on excretion urography, led to the correct diagnosis of multiple, partly laminated stones within a pyonephrotic kidney.

Case 3. A female, aged 45, gave a history of recurrent attacks of epigastric discomfort for three months, the attacks lasting from three to four hours, and not related to intake of food. The patient was markedly obese, weighing 187 pounds. Two months later, she developed pain over the spine, located from the first to the ninth

thoracic vertebra, and radiating anteriorly toward the xiphoid process, but never to the shoulder region. There was a moderate loss of weight. No abdominal masses were palpable. The patient was constipated and at times the stools were clay-colored. *Clinical diagnosis of gall-bladder disease was made.* One month later, a typical gall-bladder attack was observed, and the patient was hospitalized. *There were never any urinary complaints.*

ows" showed a moderate contractibility; the medial one did not present any change in its size. In addition, a perfectly round laminated stone the size of a cherry was seen "in the area of the bile ducts." A considerable amount of non-resorbed dye within the hepatic flexure of the colon was noted.

Considering these unusual roentgenographic findings, a flat plate was taken three days afterward (Fig. 3-*c*) which re-

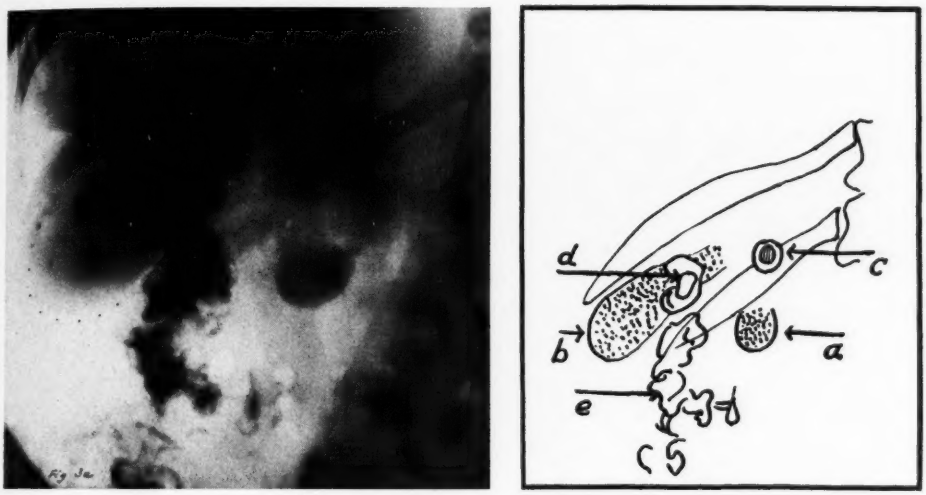
Fig. 2-*c*. Case 2. Excretion urogram shows gross enlargement of all calices and of the kidney pelvis. The group of laminated concretions is lodged within the lowermost minor calix; dye secretion into this calix is greatly delayed. The branched stone is located in the middle calix. The intrarenal location of all the stones was corroborated on stereoscopic studies.

Roentgenographic Study (double-dose oral cholecystography).—This revealed a most unusual picture (Figs. 3-*a* and 3-*b*). In our first interpretation we strongly considered the rare congenital anomaly of two gall bladders, one located laterally, the second in the usual place. Twenty-eight such cases with five roentgenographic visualizations have been reviewed by Gross (7), and the findings on our film seemed compatible with his anatomic drawings. Following administration of a fat meal, the lateral of the "two gall-bladder shad-

vealed that "the stone within the bile duct," the "medial gall bladder," and part of the "contrast dye in the hepatic flexure" were, in fact, large calcifications within the right kidney. Additional studies in the lateral and antero-posterior direction proved that the calcifications were lying close together and far posteriorly. The wide clearance between the concretions, seen on the postero-anterior view, was an artefact, being caused by the marked obesity of this patient, whereby the stone area was placed at a great distance from the

film and consequently appeared distorted. A pyelographic study was strongly advised but was refused. Because of the typical clinical symptomatology of gall-bladder disease, a cholecystectomy was performed. The gall bladder showed cholesterin deposits on its walls (strawberry gall bladder) and a mild chronic cholecystitis. *No stones were found within the gall bladder or in the bile ducts.* Following surgery, however, the symptoms were not relieved and the patient was re-admitted. Urinalyses repeatedly revealed an acid reaction and small amounts of albumen. The leukocyte count was 25,000 to 35,000, and occasionally there were a few red blood cells. Bacteria were constantly absent and repeated cultures showed no growth. Retrograde pyelography (Fig. 3-*d*) was then done and revealed a perfectly normal ureter, kidney pelvis, and lower calices on the right side. However, the middle and upper minor calices formed large cavitations which were reached through very narrow infundibula and which contained the calcifications lying close to the surface of the organ. The advanced disease over the upper half of this kidney was in striking contrast to the normal appearance of its lower half. The opposite kidney and ureter were normal. A definite diagnosis of multiple kidney concretions and widening of the calices in the upper half of the right kidney was thereby established.

The right kidney was finally removed by Dr. H. Rolnick, and showed that several of the calices were dilated and filled with brittle smeary green-brown material containing distinct concretions. In the vicinity of the upper pole, there was present a bulging area, 2 cm. in diameter, which contained a round concretion, a pyogenous membrane, and yellowish thick material resembling exudate. *It did not communicate with the kidney pelvis.* No sign of tuberculosis was found.



Figs. 3-*a* and 3-*b*. Case 3. Oral cholecystography. Preliminary erroneous impression was that of congenital double gall bladder: (*a*) medial gall bladder, (*b*) lateral gall bladder, (*c*) combination stone in the gall-bladder neck or cystic duct, (*d*) and (*e*) non-resorbed contrast dye within the colon. Final correct interpretation: (*a*), (*c*), and (*d*) are concretions within the right kidney; (*b*) is the normal gall bladder (see Figs. 3-*c* and 3-*d*).

Summary.—An obese patient exhibiting the clinical picture of gall-bladder disease and never having complained of urinary symptoms presented, on cholecystographic study, a film suggestive of a double gall bladder and a typical laminated biliary duct stone. This erroneous impression was

immediately rectified and the diagnosis of multiple renal concretions within localized dilatations of the upper and middle minor calices of the right kidney was established. The gall bladder was removed and failed to show any concretions. Later, right nephrectomy was performed and the kidney showed the presence of three large renal concretions. The gall-bladder symptomatology was satisfactorily explained through the finding of a strawberry gall bladder, with chronic cholecystitis.

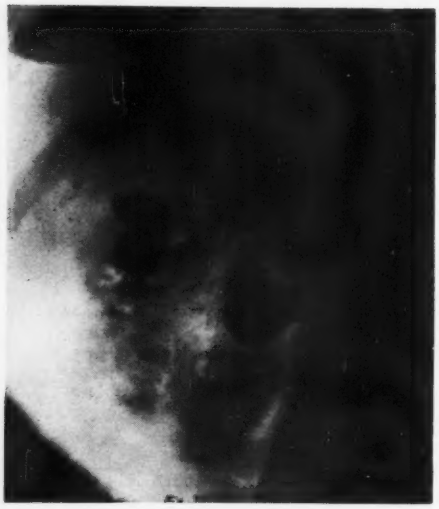


Fig. 3-*c*. Case 3. Flat plate of the gall-bladder region (taken three days after that shown in Fig. 3-*a*) following complete elimination of the gall-bladder dye shows the presence of three large concretions.

DISCUSSION

Excellent anatomic illustrations of laminated renal stones are found in many textbooks on urology and pathology. Generally, with laminated stones a small organic nucleus is found, surrounded by a large colloid-crystalloid substance composed of uric acid, xanthine, or cystine. The peripheral shell consists of calcium oxalate or phosphate, rarely of calcium carbonate (4, 8, 9).

While the general problems of stone formation are beyond the scope of this paper, a discussion of the lamellar formation of certain concretions will be of value. It is assumed that the complication of infection with the presence of an aseptic calculus plays the dominant rôle in lamellæ formation (4, 8, 11, 14), and is analogous to the "infectious combination stone" of the biliary system. Through disturbance of the pH in the urine and changes in the equilibrium of the protective colloids, precipitation of the crystalloids and formation of calcified deposits upon the surface of the stone already present are facilitated. According to Kjellberg (14), stasis may be regarded as an important factor. No satisfactory explanation can be given for the fact that the laminations so frequently observed on anatomic specimens so rarely reach a sufficient intensity as to become roentgenographically demonstrable. It may be that encystment with lack of drainage of the calix which harbors the stone is a contributing factor. In our patients, the stone was encysted once and the infundibula of the involved calices showed a conspicuous narrowing in two cases, justifying the conclusion that drainage was temporarily or permanently interfered with. In the future, if surgical specimens of such kidneys are obtained, it would be worth while to examine for insufficient drainage, to study separately the reaction of the urine in the involved calix and in the remaining portions of the urinary tract, and to make separate chemical analyses of the different layers of the laminated stones.

Roentgenologically, the problem of laminated kidney stones has been somewhat neglected; as late as 1937 Hanley (9), in reporting one such case, made the following statement: "After an extensive survey of the entire literature, I have been unable to find a single contribution in respect to laminated kidney stones." His published case demonstrates perfectly laminated stones which from their shape leave no doubt as to their renal origin. Eisendrath and Rolnick (4) also show a similar illustration of stones with distinct lamellations but otherwise typically of renal appearance. In illustrations published by Lauber (15), Kjellberg (14), and Eisendrath

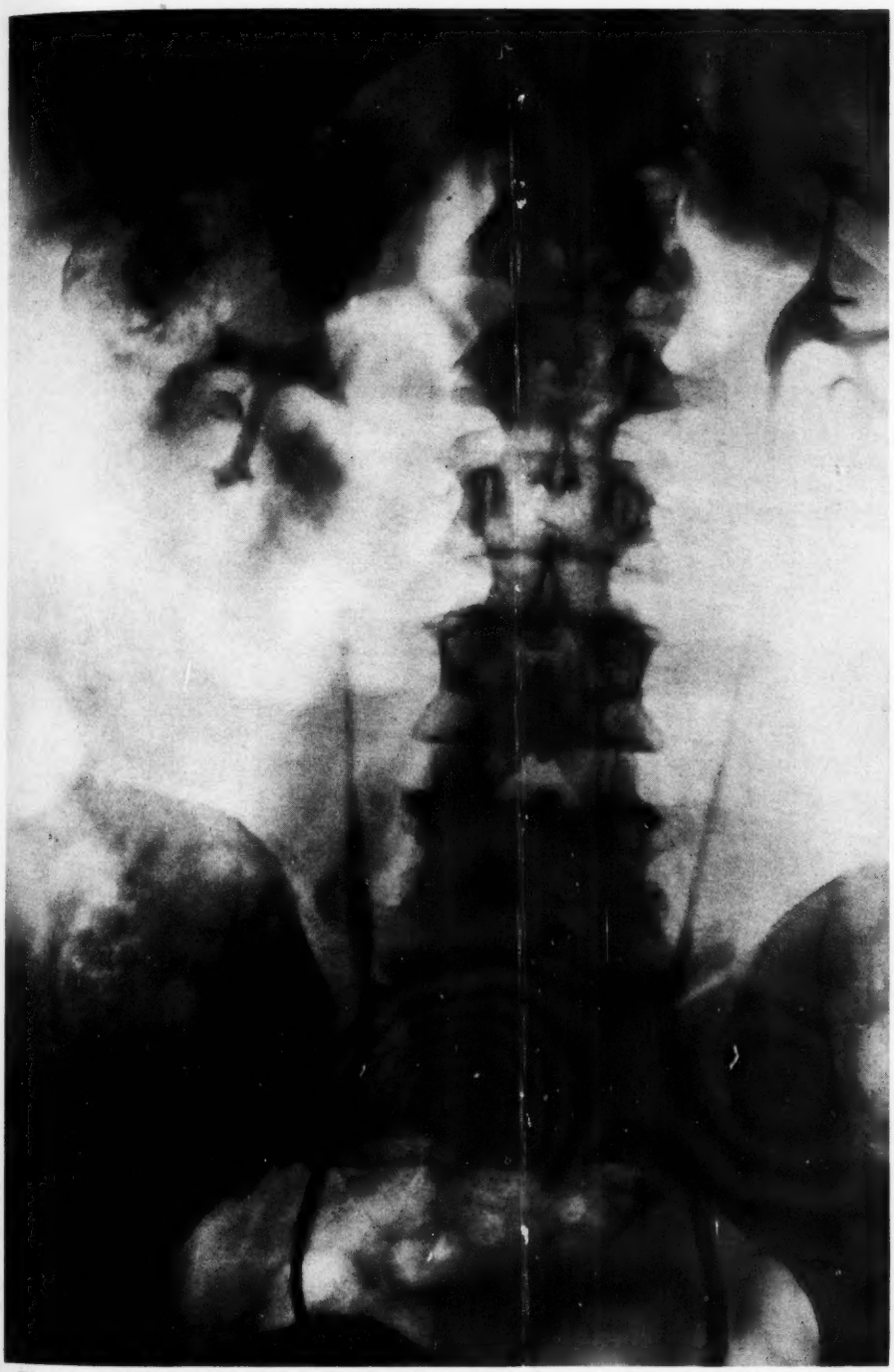


Fig. 3-*d*. Case 3. Retrograde pyelography. The concretions are lodged in outpouchings of the upper and middle minor calices. Lower calix, kidney pelvis, and ureter are of normal appearance. Following surgical removal, it was seen that the laminated combination stone was encysted, and the calix did not communicate with the kidney pelvis. There was no evidence of tuberculosis.

and Arens (5), lamellations are clearly visible but do not create differential diagnostic difficulties. The only four instances in which shape, position, and lamellar structure of kidney stones are such as to suggest biliary concretions, are the case of Potter (17), one illustration (Fig. 26) of Lepennetier and Nadal (16), one (Fig. 11) of Lauber (15), and the "hollow stone" of Cecil (2). Lepennetier and Nadal's illustration is particularly misleading and simulates a gallstone perfectly. Considering this scarcity of illustrations, we are adding a composite picture which shows the concretions in our three cases in original size (Fig. 4).

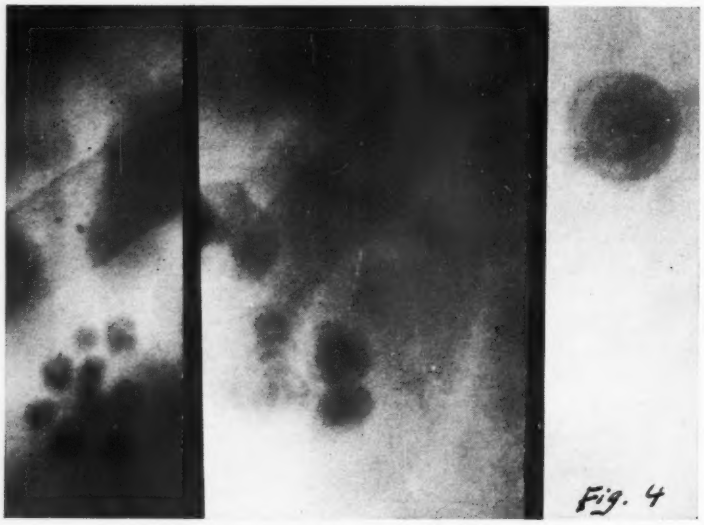


Fig. 4. Composite picture in natural size, showing all the concretions observed in the three cases recorded. All these stone shadows were produced by kidney concretions, none being within the biliary system.

Beside lamellar structure, facet formation of renal stones has also been observed (14, 17, 22) which, according to Kjellberg, is produced "if a certain movability of the stones in their cavity against each other is guaranteed."

It is my opinion that these few publications fail to give a true account of this differential diagnostic problem, and that such instances where kidney stones closely simulate biliary concretions are not as rare as formerly thought to be. Textbooks, dealing with this problem, generally, give such statements as the following: "solitary or multiple ring shadows with transparent centers when found over the right side are produced by gall stones and present little difficulty." In view of the problems encountered in these reported cases we can hardly support such definite statements. The roentgenologist should not commit himself too lightly and should view with suspicion even the "typical case."

CONCLUSIONS

(1) The fact that kidney stones may closely simulate biliary concretions in their roentgenologic appearance has not been sufficiently emphasized in the literature. There is a scarcity of illustrations of such cases.

(2) The attempt to differentiate whether roentgenographic stone shadows accidentally observed on a flat radiogram, are of urinary or biliary origin, will lead to a certain percentage of errors even in instances in which the stones present a "typical structure and arrangement."

(3) Three cases of "typical gall-stone pictures" produced by kidney concretions are analyzed and illustrated.

(4) These cases suggest that laminated kidney stones may be formed, usually in calices with disturbed drainage, under conditions in which an infection complicates the picture of a stone already present.

(5) Tuberculosis was not found in any of the cases and urologic complaints were absent or minimal.

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THE EVALUATION OF CANCER STATISTICS BY CORRELATION ANALYSIS[1]

By LEWIS G. JACOBS, M.D., *Winona, Minnesota*

AS the therapeutic attack on cancer has improved, it has been increasingly difficult to evaluate the numerous conflicting reports advocating the use of various forms of therapy. Men whose honesty and ability are beyond question favor divergent therapeutic approaches to the same disease. In seeking the reason for this difference of opinion, one is forced to the conclusion that the basic difficulty is the evaluation of the statistics; which difficulty in evaluation is dependent on the fact that the differences in results are of the order of 10 per cent, a magnitude hard to demonstrate with any but the largest series and most exact methods. Most of the methods for the analysis of cancer statistics in current use, however, are of an elementary sort, and not well adapted to the purpose of showing such small differences. This is particularly emphasized by observing that the composition of no two series is the same or even reasonably similar, and, therefore, the decision as to whether or not an observed difference in results is significant takes on unusual unreliability. A complete study, on the other hand, will avoid this difficulty to a large degree, as will be shown, and will permit more satisfactory comparison of results.

In 1936, I published an article (3) advocating the use of survival curves in the analysis of cancer statistics. While the idea has merit, and has been used (it was independently suggested and employed by Nathanson and Welch, 5, and by Lewis and Rienhoff, 4), its limitations have been increasingly clear, especially as concerns comparisons. My belief at that time was that mathematical analysis was not suitable for the problems involved, but further study has led me to consider that this opinion was, to a large extent, incorrrect. On trial, it has proved that graphical analyses which make no assumption concerning the type of relationship present demonstrate a close correlation[2] between some of the data obtained from the patient and his length of life after treatment. Predictions of life span based on these graphical relationships are in good agreement with the observed survival. While we are not greatly concerned with the prediction of life expectancy, the degree and kind of relationship between this and the various conditions that change it are of paramount interest, since in a consideration of these relationships a more precise basis for comparison is available than can otherwise be found. In order to demonstrate this objectively, I have performed such an analysis on data published by Geschickter and Copeland (2), on osteolytic sarcoma. The conclusions here reached are my own, and, I think, of some importance.

Space permits only a brief résumé of the method; a complete description with working examples may be found elsewhere (1). One is usually desirous of finding how much certain "factors" influence a "result." For instance, how much do (*a*) the patient's age, (*b*) the dose of radiation, and (*c*) the anaplasia of the tumor influence (*d*) the length of life? We call *d* the "dependent variable" since it is considered as being a resultant of *a*, *b*, and *c;* these last are termed "independent variables." One must, first of all, designate precisely how each variable is measured; for instance, we might well decide to measure length of life as the time of survival following the first treatment. One then plots for each patient the value of *d* against the value of

[1] Presented before the Twenty-fifth Annual Meeting of the Radiological Society of North America at Atlanta, Dec. 11–15, 1939.

[2] By "correlation" is meant the extent of a relationship between two or more variable factors, *i.e.*, how much changes in one are associated with changes in others. The process of determining this relationship is termed "correlation analysis."

the independent variable one guesses to be the most important, say b in this instance. When all the dots are plotted, a free-hand curve is fitted to them as well as possible. It is sometimes easier to fit the curve if, in addition, the average positions of groups of about 10 cases are plotted also, since such averages usually tend to fall more clearly into a pattern than the individual observations. Next, the algebraic deviation of each dot from the curve (that is, the difference plus or minus between the actual observation and what one would have guessed it would be from the curve) is computed, and these differences are used as a new dependent variable with another of the independent variables, say c. When similar deviations from the second curve have been calculated, they are used with the next variable for a third curve, and so on until all the independent variables are exhausted, however many. In cases in which no numerical value can be assigned to an independent variable, the average deviation of the group (having regard to the sign of each observed deviation) is used as the "guessed" value instead of a reading from a curve. When the last variable has been used, the remaining residuals are squared, the average of the squares computed, and the square root of the average taken. This value is called the "standard deviation" (sometimes "root-mean-square deviation") of the correlation. From this value, and the standard deviation of the individual values of d from the mean value of d, is calculated the "index of correlation," which measures the extent of the relationship.[3] Then, returning to the final residuals again, one uses them with the first studied independent variable

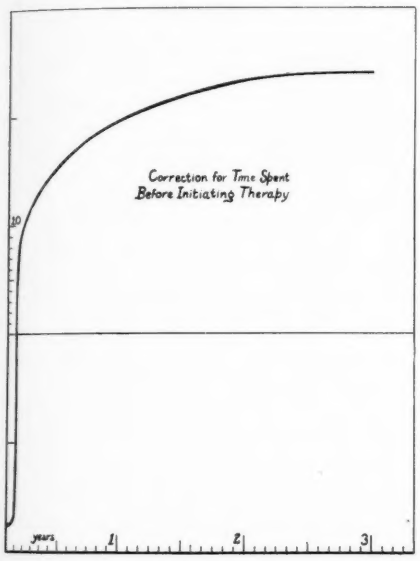

Fig. 1. Relation between time lost before starting therapy (abscissa) and the addition or subtraction from expected survival (ordinate, scale in months). Note that the fastest rate of change occurs between the first and second months.

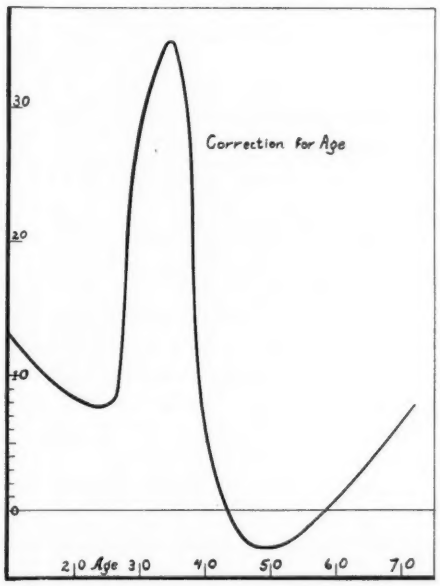

Fig. 2. Relation between age (abscissa) and correction to life expectancy. Note maximum at 34 years and minima at 24 and 49 years.

[3] The mathematical expressions for these calculations are:

$$1.\quad \sqrt{\frac{\Sigma d^2}{N}} = \sigma_d \qquad 2.\quad \sqrt{1 - \frac{\sigma_d^2}{\sigma^2}} = \rho$$

Where d is the individual deviation, Σd^2 the sum of the squares of the deviations, N the number of cases, σ the standard deviation of the observations, σ_d the standard deviations of the residuals, and ρ the index of multiple correlation.

to correct the first curve; the easiest way to do this is to plot them as deviations from the curve, and change the shape as indicated. Then the new residuals are calculated and used with the second curve, and so on. When this is completed, the new standard deviation and index of correlation are calculated; if the standard deviation has decreased, the whole process is repeated, and these cycles are continued until the value of the standard deviation ceases to diminish or begins to rise. This usually means from four to six cycles. The curves giving the smallest standard deviation are taken as the final ones, and the values of the standard deviation and index of correlation are corrected for the number of cases and the number of variables. These final results may then be used for interpretation and comparison.

TABLE I.—DEVIATION FOR SEX

Male	−0.8
Female	+2.3

TABLE II.—DEVIATION WITH LOCATION

Involvement of trunk	+8.9
Involvement of proximal joint	+2.4
Involvement of distal joint	−0.5

In the problem at hand, the first pair of variables considered were survivals after the beginning of therapy (dependent) and the time lost before the patient first came for care. The final curve (Fig. 1) shows that the longer the patient waited, the *better* his chances, most of the change in outlook taking place rather suddenly between one and two months. This seems a very anomalous conclusion, and an explanation must be found. The most obvious, and probably correct one, is that the natural growth speed or malignancy of the tumor is highly correlated with the time it requires before beginning to trouble the patient, and, consequently, the curve we have determined is really more a measure of the malignancy of the tumor than the effect of delay. Thus the bad effect of delay is masked. (No measure of malignancy apart from this could be included in this series, as the data obtained from the reference were not sufficiently complete in this respect.) Perhaps, also, one could speculate that patients who have carried a tumor for a long time develop an immunity to it, and after treatment do a better job of mastering the residua than those who have not had a chance to develop immunity. It is not impossible that still other factors may enter into the explanation. While the first suggestion above stated has a high degree of plausibility, a complete study with this point in mind would certainly be profitable.

TABLE III.—DEVIATION WITH FORMS OF THERAPY

No treatment	− 1.6
Amputation only	+ 2.2
Curettage only, or biopsy	+ 6.1
Irradiation only	+17.7
Biopsy, then amputation	+19.8
Amputation and irradiation	+ 6.9
Biopsy, amputation, irradiation	+19.9

The life span after treatment has a decided correlation with the age of the patient at the time of beginning treatment, showing minima at 24 and 49 years and a maximum at 34–35 years (Fig. 2). The significance of this peculiarly shaped curve is not clear; it might not be unreasonable to expect better results in early adult life, rather than in the fourth decade; while the improvement in outlook in old age is also somewhat surprising. This finding should lead us to examine more closely the truth of the traditional dictum that cancer in young people is more than ordinarily malignant. There seems to be some hitherto unsuspected and much more complicated relationship with age, although its exact nature can hardly be predicated on so small a series as this.

Three variables, sex, location, and form of treatment, were not quantitative in nature, and were studied by group averages of the residuals. In this series women fared slightly better than men, living about three months longer, when the effects of other variables were allowed for (Table I). Location (Table II) showed a reversal of the expected trend, the more proximally located tumors proving to be less imme-

diately fatal than the more distal; but most of the cases were in the femur or humerus, and the size of the other two groups is so small as to cast doubt on the validity of this conclusion. It is not at all unlikely that such an observation might have arisen through the chances of sampling, and further samples might show the opposite, or expected, relationship. The correlations of therapy (Table III) are in a similar case; the figures show that amputation or curettage is better than no treatment, and that irradiation or a combination of several procedures is better still. But as the majority of the cases fell in the amputation group, it is quite possible that no real difference, or a reversal of the observed difference, might be observed in a better balanced series. Thus it is clear that the composition of the series is defective in these respects, and another attempt should be made with more attention given to securing a fairly even distribution of the sample.

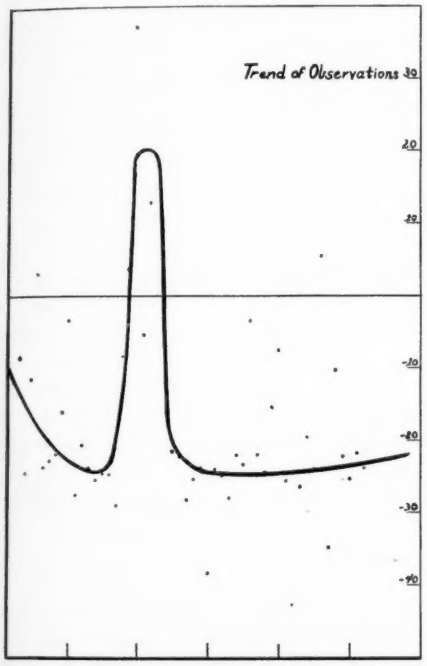

Fig. 3. Trend of the observations. Most of the "hump" in the middle is caused by four dots (patients) only.

The "trend" of the observations is the correlation between time and results. As the curve (Fig. 3) shows, a period of increasingly poorer results was followed by a marked improvement, only to give way to another period of poor results. But upon looking at the individual cases, it is seen that most of the spurt was due entirely to four patients who did unusually well; if these are omitted, there is only a very slight trend correlation. This would suggest, of course, further examination of the data to see if some factor has been disregarded, which might explain the good result in these four cases. In the present instance there is no further information available to give such an explanation, but there may be some one of the many factors not taken into account which would explain the finding. The trend curve thus serves to act as a check on some of our conclusions; of course it would also show real changes in results due to improvement in experience and technic. In this particular instance, the changes in therapy over the period studied were apparently negligible; and in agreement with this is the flatness of most of the trend curve.

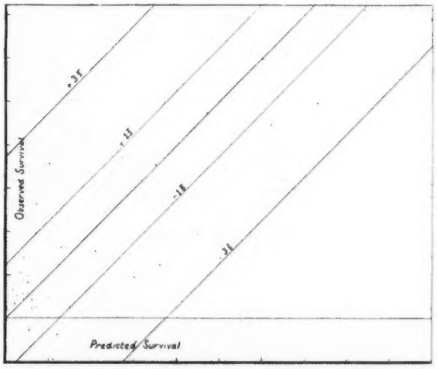

Fig. 4. Dot chart to show correlation. The central line is the so-called "regression" line or a perfect agreement between prediction and observation. Most of the cases in the longer-lived group fall on or below the prediction line. Scale in 10-month intervals.

Finally, the scatter chart (Fig. 4) to show the relation of the observations to the predictions demonstrates the degree of correlation. It is evident that our predictions

are on the whole accurate, although in the longest-lived patients the predictions tend to be too large. If more cases were in this part of the series, it would be worth while to introduce a further correction, since it seems evident from these data that some sort of joint relationship exists in which, when all the factors tending to produce a longer survival operate together, they are individually somewhat less effective than when only one or two of them operate. But the element of error introduced by neglecting this is no larger, or may even be smaller, than the error in estimating the extent of this effect from so few cases. As it is, the raw coefficient of correlation is 0.915 and the raw standard error of estimate, 9.8 months; when these are corrected for the small number of cases and the large number of variables, the correlation probable for all such cases is 0.861 and the corrected standard error of estimate, 12.5 months. Only eight observations were different by more than one standard error from the predicted value. Of the variation in length of life, 74 per cent has been accounted for by association with the factors studied. This is quite a good agreement for a biologic problem; that of oxygen consumption with surface area and age (basal metabolism) is in the same neighborhood.

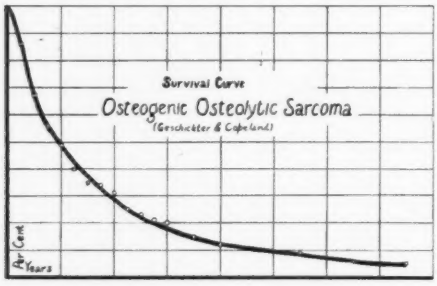

Fig. 5. Survival curve. Note slight irregularities due to paucity of cases.

Turning now to the survival curve (Fig. 5), which is constructed from the same group of cases plus those still living, we find that about 5 per cent of the patients survived seven and one-half years, while 9 per cent survived five years. Five-year survival, then, is in no sense a measure of being "cured," since nearly half of those alive at five years died in the next two and one-half years. When the data are replotted to show the number of patients dying in each of a number of equal periods (Fig. 6), it is found that—using a three-month grouping—most of the deaths occurred between the third and the twelfth month. The importance of using a small enough interval is demonstrated by replotting with a six-month grouping; here one would feel that most of the deaths had occurred in the first six months, and, therefore, would be inclined to conclude, in the absence of specific knowledge to the contrary, that they were due to the therapy itself. This conclusion would evidently be incorrect.

For the sake of completeness, charts showing the age incidence and the number of patients coming for treatment after given periods of obvious symptoms are shown (Figs. 7, 8). These charts are self-explanatory, and have long been used in analyzing such statistics; the age distribution, with its peak in early adult life, and the occasional occurrence of delay beyond a year in seeking treatment are both factors well known and often commented on. Similar distribution charts are, at times, useful for the study of other factors; to determine how one series compares with another in composition, or how the composition of the series compares with that of the general population. Their use must be dependent on the object of the study. A tabulation of the data on the individual patients is here omitted, since it has already been published in the book cited; however, this is essential to any serious report, since unless these data are permanently recorded the article is of almost no value for future comparison, particularly by newer methods which time will doubtless produce.

What, then, have we discovered from our study? First of all, we have a comparison between several forms of treatment

in which the effects of several other factors known to have a marked influence on the result have been removed. The conclusion is that the poorest results are secured by no treatment; amputation, curettage, or biopsy alone seem to lead to somewhat better results, while irradiation, or a combination of several procedures either with or without radiation, yields the most favorable result. While there is admittedly doubt as to the validity of the conclusion in this particular series, the doubt is due to a very obvious defect, the fact that most of the cases were treated by one method (amputation) and the numbers treated by other methods were, consequently, too small for reliability. In another series this defect could be avoided. Had our conclusion been based on such a series, it could be accepted as highly probable or even final; as it is, we may say that it is suggestive but not proved. In the second place, some observations which did not agree with our preconceived notions have turned up in the study of the effect of age, of delay before coming for treatment, and of location of the tumor. While it is possible that the reasons for some of these anomalous results have been correctly guessed, more study is certainly indicated. An increase in the number of variables to include others which might have bearing on some of these points seems desirable; particularly the degree of pathologic malignancy (as by Broders' grading) and the extent of clinical involvement suggest themselves. Lastly, it is shown that some of the previously used methods give information not obtained by this method, and must, therefore, be retained in a complete analysis. The five-year cure rate again appears more deluding than helpful, since it is clear from the data that no real comparative information is obtained by stating that there were 9 per cent five-year survivals. It must be noted that the results of this mathematical analysis apply rather to palliation than cure, from the method of selecting the cases, but this essential limitation of the method is partly compensated for by the survival curve, and in series which have large enough numbers of survivors this defect may be eliminated by a separate analysis.

In conclusion, a complete mathematical analysis which employs every possible mathematical tool gives much more information in such problems as the one here treated than does any partial approach; and by using such methods as here described it seems likely that many of the

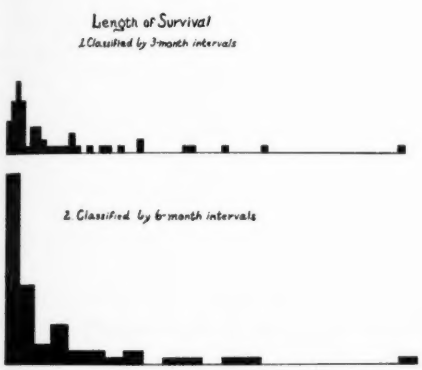

Fig. 6. Classification of cases by length of survival.

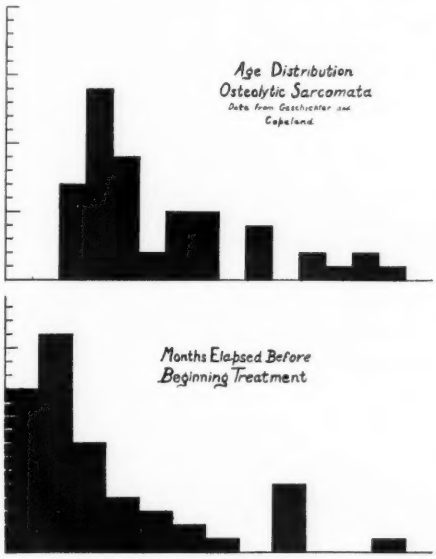

Fig. 7 (*above*). Age distribution of patients.
Fig. 8 (*below*). Delay before instituting treatment; scale in three-month intervals.

outstanding perplexities about the behavior of cancer patients may be determined as resulting from other well known factors in the picture; particularly evaluation of treatments advocated should be possible. Since the only other intelligent approach to this last problem, the treatment of alternate cases, using one group as controls, has been almost abandoned as impractical, this possibility assumes great importance.

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DISCUSSION

R. R. NEWELL, M.D. (San Francisco): I have been much interested in Dr. Jacobs' attempts to make use of statistical computations in order to try to obtain the maximum information from clinical experiments. Even when a student, Dr. Jacobs evinced a willingness to undertake the difficult job of doing statistical work and statistical mathematics. I have been trying to keep him pepped up to the project since then. He was kind enough to let me have a copy of his paper, which I went over as carefully as I could, and I would like to make some comments.

In this case, Dr. Jacobs has chosen a disease nearly always fatal; so early treatment, within the range of its being diagnosable, is of no avail. I judge his explanation correct as to a positive correlation between delay and longevity.

One cannot expect a correlation coefficient of 0.8 to mean as much for this system of graphical analysis as a Pearson product-moment coefficient of 0.8. In the latter we have limited ourselves at the outset to straight line relationships. A second sample, if we analyzed it the same way, could give only another straight line, differing, perhaps, in origin and direction.

But, with Dr. Jacobs' graphical analysis, not only could the origin and shape be different, but also the shape of each of his regression curves could be changed. Put another way, the analytical method chosen by Dr. Jacobs has a remarkable ability to follow even obviously capricious variations in the trend of data.

The minimum number of cases considered significant for a product-moment correlation is usually taken at 25, if data are well scattered. But I should think a much larger number needed for significance by the method Dr. Jacobs has used.

I do think this and perhaps other methods of statistical analysis offer much in the study of our therapy problems. We ought to record possibly significant data quantitatively for large numbers of patients, and then let enthusiasts, like Dr. Jacobs, have them in their raw state to see what can be extracted.

It may be that the method of study described will free us from the necessity of keeping all our therapy factors absolutely constant, except the one we wish to study. I mean, it is hard to collect a large series of cases of a single disease treated in just one way to compare with another series treated another way. We feel we are doing our patients an injustice if we make no use of clinical experience, but stick to last year's method in spite of everything. But the data do have to be recorded accurately and made available to the statistician.

K. WILHELM STENSTROM, PH.D. (Minneapolis, Minn.): It seems to me that Dr. Jacobs has brought to our attention a highly important problem. We are usually trying to prove the effectiveness of a certain type of treatment by means of results obtained in a group of patients. Consequently, we are using statistical methods. It should, then, be evident that the better

we utilize available statistical methods, the more reliable the conclusions will be.

Statistical methods have been developed to a great extent and we have been slow in adopting them for therapy. Statistics, of course, is a science in itself, and it may take too much of our time and effort to become thoroughly familiarized with it. Therefore, it seems that we should get the help of statisticians and give them the close co-operation necessary because they need information concerning the clinical aspects before deciding how to tackle the problem mathematically. The few radiologists who master statistical methods are the best qualified to show us how the figures available may be used.

Because we are not so well acquainted with these methods as Dr. Jacobs, it is a little difficult for us to follow the details and to offer reasonable criticism.

It should be emphasized that the particular method used by Dr. Jacobs is not always applicable and that a certain amount of testing and judgment has to be used. The particular study to which Dr. Jacobs has referred here has led to several interesting considerations which were not evident before the calculations had been carried out.

One of the unexpected findings was that the patients who came for treatment soon after the onset of the disease showed a shorter survival than those who had had the disease for a longer time. Dr. Jacobs explains this finding in a rational manner.

I should like to mention that when we analyzed cases of carcinoma of the breast treated in our department recently, a separate analysis was made of those patients who had had an apparent onset of the disease a month or less before the first treatment, whether surgical or radiological. These patients were then subdivided into two groups. One group comprised those patients who came to us after recurrence had appeared, and these patients had a shorter survival than any of the other groups. This indicates a fact similar to the one Dr. Jacobs brought out and is probably explained in the same way, namely, that it probably represented the patients who had the most malignant type of carcinoma.

I agree with Dr. Jacobs that more information can be obtained when statistical methods are used which permit a consideration of several important factors (or independent variables) separately, if that can be done. This cannot be done unless enough data are available.

If we do not know how to use these statistical methods, we can at least try to collect the necessary data. We can still use simpler methods, and it seems to me that curves showing the survival are quite useful. These curves are so simple to construct that we can all use them. They give considerably more information than just the three- or five-year survival figures which are usually given.

I do hope that everybody who is carrying out a considerable amount of therapy work will contribute, as far as possible, to building up enough statistics, with the data carefully given; and that they at least use the survival rate curves. We certainly ought to encourage more complete statistical analysis, and we should be grateful to Dr. Jacobs for pioneering in this field.

LEWIS G. JACOBS, M.D. (*closing*): Dr. Newell was asking how much work this is. It is a lot of work, and yet it is not much work. The actual labor, physical labor, of doing the job is a tremendous task, but it does not require a lot of special knowledge to do it. To understand the theory of it requires extended mathematical knowledge but the theory is not necessary in order to do the analysis. You can learn the mechanics if you know simple arithmetic. It takes hard work to turn out the analysis; it can be shortened by the use of machinery, but I am in a small town and use longhand.

Dr. Newell questioned the value of the correlation coefficient in this particular type of analysis. It is not precisely known how valuable this is, how reliable it is; but it is thought, and there is a certain amount of experimental evidence to sustain this

belief, that the corrected correlation coefficient (it is possibly recalled that I gave the raw coefficient as 0.915 and the corrected one as 0.861) is almost the same as in the product-moment method so far as reliability and interpretation are concerned. There have been controlled series, by some of the men who have developed this method, drawn from the same group of experiments run in parallel to prove this point. That is not a rigid mathematical proof, but it is at least highly suggestive.

Dr. Newell mentioned that I had picked a practically 100 per cent fatal disease to analyze. Of course, the exact form of analysis has to depend on what you happen to choose. This was one of the few problems on which I could get data, so I picked it of necessity, not because I thought it was a good one to analyze.

Dr. Stenstrom has mentioned survival curves. It is true that they are extremely easy to construct and most useful in this type of work. However, they are extremely limited as to comparison. I do not advocate that we drop them—I think we should keep them as a part of our statistical analysis.

I am greatly indebted to both Dr. Newell and Dr. Stenstrom because they have both given me much advice on this subject.

MONOMELIC MEDULLARY OSTEOSCLEROSIS OF UNKNOWN ETIOLOGY[1]

By THOMAS HORWITZ, M.D., *Philadelphia*

THE purpose of this communication is to report an instance of sclerosis of the bones of a single limb, representing a benign lesion of bone which differs from other osseous lesions. A review of the literature suggests that this skeletal lesion has not hitherto been classified.

The following features were noted: (1) The bony changes are limited to certain of the osseous derivatives of the affected limb bud, and specifically to the ischium, pubis, femur, patella, tibia, and astragalus. The disorder is, therefore, monomelic in its distribution. (2) The lesions are asymptomatic and unassociated with deformity and alterations in length of the involved bones, and there are no changes evident in the non-osseous structures of the affected extremity. (3) There are no abnormal laboratory findings. (4) Roentgenographically, the lesion appears as a diffuse osteosclerosis which is limited almost exclusively to the medullary portion of the affected bones. In some places the cortical bone is found to be thickened from changes on the endosteal side, but there is no evidence of involvement of the periosteum. Although the sclerotic process extends as far as the articular surfaces of the involved bones, there are no joint changes evident clinically or roentgenographically. (5) Histologically, there is replacement of the normal spongiosa by densely sclerotic bone of unusual architecture, consisting of compact, irregular segments of immature and adult bone arranged in a bizarre pattern.

While this osseous lesion is believed to represent a congenital or developmental disturbance localized to the primitive osteoblastic mesenchyme of the affected hind limb bud, its exact etiology is uncertain. For this reason, and because of the roentgenographic and histologic features, I have designated this skeletal lesion as "monomelic medullary osteosclerosis of unknown etiology."

[1] Accepted for publication in January, 1940.

CASE REPORT

History.—The patient, female, aged 27 years, was hospitalized on May 6, 1939, because of an acute exacerbation of a right sciatic syndrome of one year's duration, which had failed to respond to physiotherapy, non-specific protein therapy, novocaine injections, and tonsillectomy. No symptoms were present referable to the left lower extremity. The family history and past personal history were negative; the menstrual history was a normal one. The patient had a tendency to bruise easily but had not bled abnormally after the extraction of a tooth, incision of a pilonidal abscess, or tonsillectomy. She had lost 15 pounds in weight during the past year.

Examination.—The patient was well developed and showed normal secondary sex characteristics. The heart, lungs, and abdomen were normal. The positive findings were: limitation of flexion of the lumbar spine, associated with considerable lumbar muscle spasm; limitation of flexion of the right thigh, with the knee extended, to 165°; decreased right patellar and achilles reflexes; diminished sensation to pain over the outer surface of the right calf, and tenderness along the course of the right sciatic nerve in the thigh posteriorly and along its branches on the outer aspect of the leg. There were no deformities, and motion in the joints of both lower extremities was normal. Furthermore, the lower extremities were of equal length, and there was no abnormal pigmentation, subcutaneous tumefaction, or lymphadenopathy.

Course and Operation.—Roentgenograms revealed an unusual osseous lesion involving the left ischium and pubis and the left femur, patella, tibia, and astragalus,

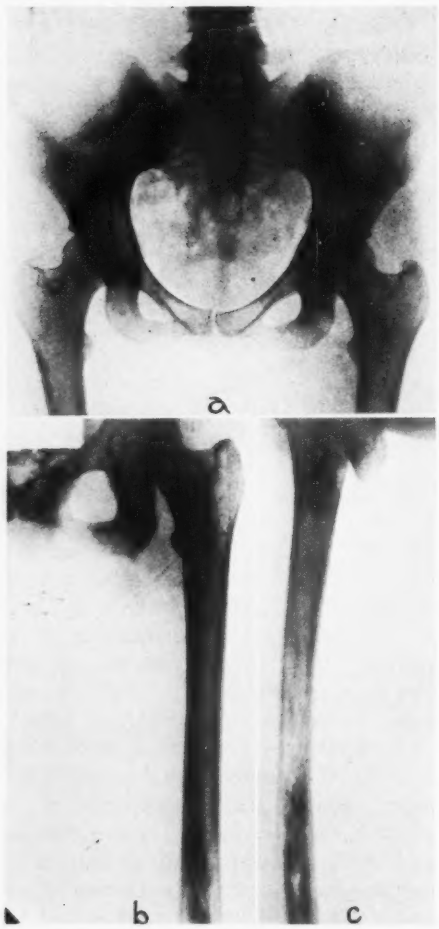

Fig. 1. (*a*) Anteroposterior view of the pelvis and both hip joints. There are mottling and increased density with slight expansion of the left ischium and the ascending pubic ramus. The sclerosis involves the head and neck of the left femur close to the inferior surface. (*b*) Anteroposterior and (*c*) lateral views of the upper two-thirds of the left femur. The sclerotic process involves the entire medullary cavity with thickening of the medial border of the cortex in the mid-shaft due to endosteal proliferation. The area of medullary sclerosis is separated in most places from the cortex by an interval of bone of lesser or of normal density. There is no expansion of the bone or other deformity.

the features of which are described later. The remaining bones of the skeleton were negative roentgenographically.

On July 5, 1939, a biopsy specimen was taken from the upper left tibia under local anesthesia. (The histologic features of this specimen will be described later.) Subsequently, the patient developed an extensive ecchymosis about the site of operation. The laboratory findings in the case were such that the ecchymosis was attributed to a subclinical scurvy dependent upon subnormal saturation of the tissues with vitamin C. After several weeks, the ecchymosis had disappeared and the ascorbic acid level of the blood was found to be normal.

The right sciatic syndrome persisted despite rest, traction in bed, and physiotherapy. Spinal taps performed on two occasions, three weeks apart, gave normal pressure readings and a negative Queckenstedt's sign, but the total protein content was elevated on both occasions, being 67 mg. and 162 mg. per 100 c.c., respectively. Myelograms, utilizing at first 35 c.c. of air and then 2 c.c. of lipiodol, revealed, on the right side at the level of the fifth lumbar vertebra, a constant intraspinal defect which almost completely occluded the lumen of the spinal canal.

On Aug. 10, 1939, an exploratory laminectomy was performed, extending from the third to the fifth lumbar vertebra. The ligamentum flavum was found to be not unduly thickened, and after incision of the dura no pathologic lesion could be noted despite a careful search. The absence of an intraspinal lesion in the presence of such definite roentgenographic findings was inexplicable. What was more confounding was the spectacular recovery after the operation, the right sciatic pain and tenderness and the right hamstring spasm lessening rapidly and disappearing completely in one week. The wound healed *per primam* without the appearance of ecchymosis. There has been no recurrence of pain or disability.

Laboratory Findings.—Repeated examinations between May 16, 1939, and Aug. 3, 1939, showed hemoglobin from 70 to 82 per cent (Dare); red blood cells from 3,990,000 to 5,300,000; white blood cells from 7,100 to 11,200, with a normal differential count.

Urinalysis was consistently normal. A

24-hour urine specimen was negative for Bence-Jones protein.

Calcium and phosphorus determinations were as follows:

Date	Serum Ca (mg. %)	Serum P (mg. %)	Serum Phosphatase (Bodansky units)	Serum Protein (gm. %)
5-20-39	11.6	3.9	6.0	...
6-27-39	9.2	3.8	3.8	7.3
8-21-39	...	4.3	4.6	...

Blood Wassermann and Kahn tests were negative; plasma cholesterol, 172 mg. per cent; blood sugar, 84 mg. per cent; blood non-protein nitrogen, 24 mg. per cent; blood sedimentation rate normal; blood platelets 432,000; coagulation time three and one-half minutes and bleeding time four minutes.

A test for vitamin C saturation of the tissues on July 11, 1939, showed no excretion of cevitamic acid in a three-hour urine specimen after intravenous administration of 100 mg. of the acid (normal excretion: 40 per cent or 40 mg.). On Aug. 7, 1939, blood ascorbic acid level 2.17 mg. per 100 c.c. plasma (normal: 0.6 to 2.5 mg.).

Roentgenographic Findings.—X-rays of the skull, entire vertebral column, clavicles and costal cage, bones of both upper extremities and right lower extremity, and of the lung-fields were negative.

Pelvis: There was mottling and increased density with slight expansion of the left ischium and the ascending ramus of the pubis (Fig. 1).

Left Femur: There was sclerosis involving the head and neck, close to the inferior surface. The sclerotic process involved the entire medullary cavity, especially in the lower third of the shaft. Although the medial border of the cortex in the mid-shaft appeared to be thickened, the area of medullary sclerosis was usually separated from the normal cortex by an interval of bone of lesser or of normal density. There was no periosteal thickening, any increase in cortical thickness being on the endosteal side. Although the intense sclerosis seemed to stop, distally, close to the site of the former epiphyseal plate, a diffuse mottling and small sclerotic patching extended as far as the distal articular surface. There was no expansion, bowing deformity, or alteration in length of the bone (Figs. 1 and 2).

Left Patella: The lateral projection showed mottling and increased density of its inner structure, the cortex appearing uninvolved except for some thickening posteriorly (Fig. 2).

Left Tibia: There was sclerosis of the medullary portion, especially involving the medial portions of the proximal and distal thirds. The dense areas seemed arranged somewhat in linear streaks running parallel to the longitudinal axis of the bone. Mottling and sclerosis extended as far as the proximal and distal articular surfaces. The cortex at the medial and posterior borders was thickened on its endosteal side, and there was no periosteal proliferation. There was no expansion, bowing deformity, or alteration in length of the bone (Figs. 2 and 3).

Left Fibula: Negative (Figs. 2 and 3).

Left Foot: There was diffuse mottling and increased sclerosis of the astragalus. The rest of the foot bones were uninvolved (Fig. 3).

Comment on Roentgenographic Findings.—The osseous lesions were confined to the left ischium and pubis, entire left femur, tibia, patella, and astragalus. The disorder involved the entire length of the long bones, reaching the articular surfaces, and the density seemed most marked in the proximal and distal thirds of their shafts toward the medial and posterior portions. There was no periosteal proliferation, and cortical thickening when present was the result of thickening on the endosteal side. In the main, the sclerosis seemed confined to the medullary portion of the involved bone, separated frequently from the normal cortex by a zone of lesser or of normal density. There was no expansion, deformity, or alteration in length of the affected bones. The joints between or adjacent to the involved bones were well preserved.

It was felt that the osseous lesions, restricted as they were to the asymptomatic left lower extremity, bore no relation to the patient's right sciatic syndrome.

Histologic Findings.—Biopsy was taken from the underlying spongiosa. The outer surface of this cortical bone was smooth and covered by periosteum of normal thickness, while its inner surface was rough. A segment of spongiosa, measuring 12 × 8 × 6 mm., was removed in two pieces. The trabeculæ were found to be thickened. The spongy structure appeared very compact, and its marrow spaces diminished in size. This modified spongiosa was of a grayish white color, and bled freely.

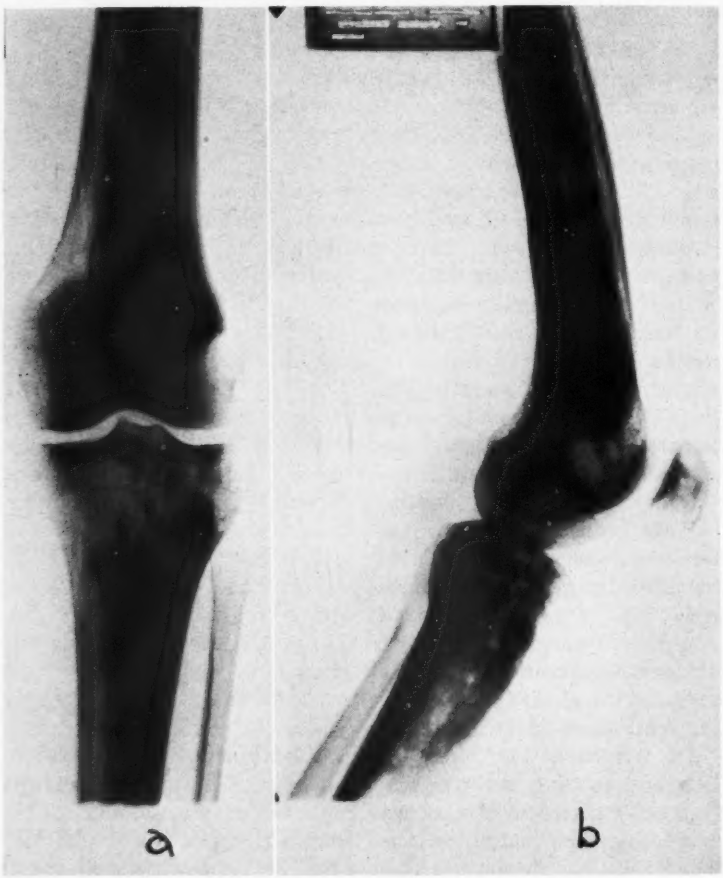

Fig. 2. (*a*) Anteroposterior and (*b*) lateral views of the left knee joint including the lower one-third of the femur and the upper one-third of the tibia and fibula. Although the dense medullary sclerosis involving the femur and tibia seems to stop close to the site of the former epiphyseal plates, a diffuse mottling and small sclerotic patching extend as far as the articular surfaces. The cortex on the posterior and medial surfaces is thickened on its endosteal side. The patella on the lateral projection shows a diffuse mottling of its inner structure, with slight thickening of the posterior cortical surface. The fibula is uninvolved.

of the left tibia from the anteromedial surface of the upper metaphysis on July 5, 1939; culture was negative.

Macroscopic Examination: The cortex was represented by a thin plate of bone measuring 12 × 5 mm. and up to 2 mm. in thickness, which was lifted away easily

Microscopic Examination: The thin segment of cortical bone was composed of normal compacta with adult lamellar structure and normal haversian systems. On its deep surface, the cortex merged into normal spongiosa, except at one point, where the compacta changed abruptly into dense bone of abnormal architecture, which had entirely replaced the local spongiosa (Fig. 4).

The abnormal bone was of unusual and irregular pattern. In some areas it was quite dense and mature, consisting of irregular segments of bone of lamellar structure joined by cement lines which were slightly heavier than those of normal bone. The vascular channels were small and encircled by concentric lamellæ. In other areas the arrangement was more irregular, there being numerous fragments of bone, some lamellated, others immature, joined together by thick, irregular, and deep-staining cement lines. The vascular channels and marrow spaces varied in size, and tended to branch and communicate. They were lined by a layer of osteoblasts and contained a few myeloid elements and some very loose connective tissue. Lining these vascular spaces was a layer of osteoid tissue which was delimited from the surrounding calcified bone by a dense thick line. In still other areas the marrow spaces were extremely large and communicated freely. The osseous structure separating these spaces was arranged as trabeculæ composed of immature bone and lined by osteoid tissue. The marrow spaces were lined by osteoblasts and an occasional osteoclast lying within a Howship's lacuna, and contained loose connective tissue, myeloid and blood elements (Figs. 5, 6, and 7).

Spinous Processes, Laminæ and Ligamentum Flavum, Third, Fourth, and Fifth Lumbar Vertebræ (specimens obtained during laminectomy Aug. 10, 1939): The cancellous structure of these bones appeared to be normal on gross examination. Microscopically, the spongiosa consisted of normal trabeculæ of lamellar bone containing occasional haversian systems and separating large communicating marrow spaces which contained normal myeloid elements. At the periphery the cancellous structure was lined by a narrow layer of normal compacta.

The ligamentum flavum from between

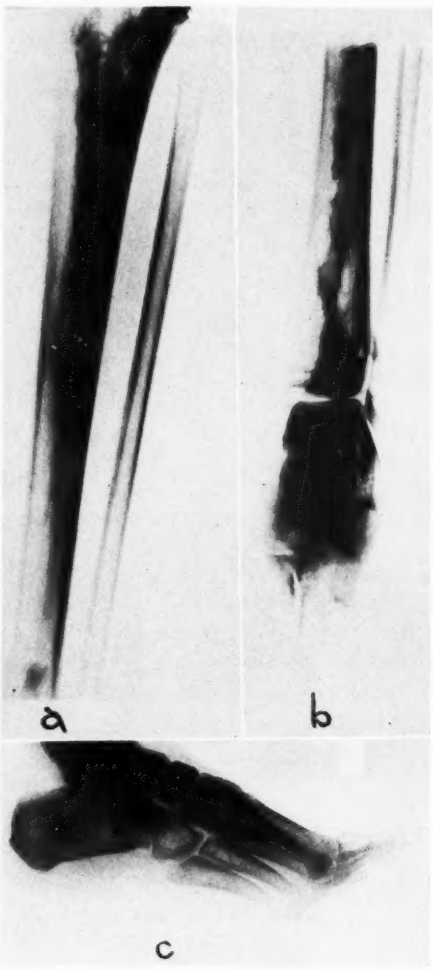

Fig. 3. (*a*, *b*) Anterior views of the left tibia, fibula, and astragalus, and (*c*) lateral view of the left ankle joint and foot. The medullary sclerosis of the tibia seems arranged somewhat in linear streaks running parallel to the longitudinal axis of the bone. Mottling and sclerosis extend as far as the distal articular surface. The cortex of the tibia, medially, is thickened on its endosteal side. The fibula is uninvolved. There are diffuse mottling and increased density of the astragalus, without involvement of the rest of the foot bones. There is no expansion or other deformity of the involved bones.

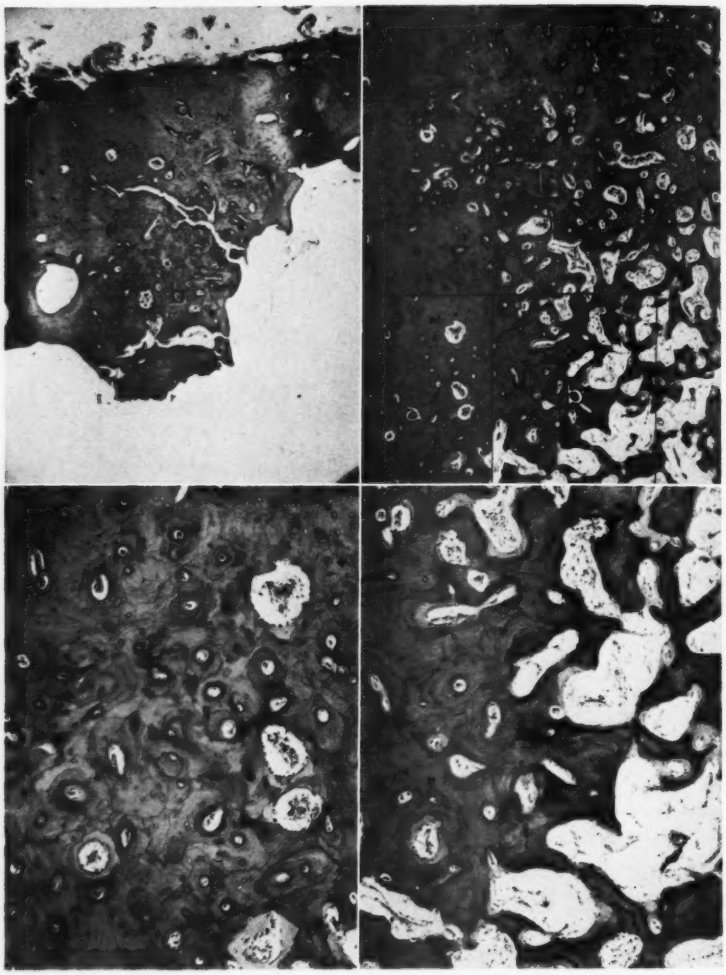

Fig. 4 (*upper left*). Photomicrograph (magnification, 25 ×) of the cortex of the tibia, removed at biopsy. The cortical bone (*a*) is composed of normal compacta with adult lamellar structure, and is covered by normal periosteum. On the deep surface of the cortex (*b*) the local spongiosa has been replaced by dense bone of abnormal architecture.

Fig. 5 (*upper right*). Photomicrograph (magnification, 25 ×) of the medullary bone of the tibia. The normal spongiosa is entirely replaced by abnormal sclerotic bone of unusual and irregular pattern, the details of which are shown in higher magnification in Figures 6 and 7.

Fig. 6 (*lower left*). Photomicrograph (magnification, 50 ×) of area blocked out as *a* in Figure 5. The sclerotic bone replacing the local spongiosa is very dense, and consists of irregular segments of immature and mature bone joined by thickened and irregular cement lines. Osteoblasts line vascular channels and marrow spaces of variable size. Some of the vascular spaces are lined by a layer of osteoid tissue which is delimited from the surrounding calcified bone by a dense, thick line.

Fig. 7 (*lower right*). Photomicrograph (magnification, 50 ×) of area blocked out as *b* in Figure 5. Here the marrow spaces are very large and communicate freely. The osseous structure between these spaces is arranged as trabeculæ composed of mature and immature bone and these trabeculæ are lined by a layer of osteoid tissue. The marrow spaces are lined by occasional osteoblasts, and contain loose connective tissue, myeloid, and blood elements.

the fourth and fifth laminæ was approximately 5 mm. thick. Microscopically the specimens were found to be composed of bundles of collagenous fibers with small nuclear elements and occasional vascular channels. There were no inflammatory cells, no hemorrhage, pigmentation, or evidence of degeneration.

Comment on Histologic Findings.—In the biopsy specimen from the tibia, the osseous changes were limited essentially to the spongiosa. The normal cortical bone was separated by an interval of normal cancellous bone from the abnormal spongiosa, except at one point where the compacta merged abruptly into abnormal bone. There was distortion of the haversian systems and a marked increase in the interstitial osseous tissue—evidence of lively bone deposition. On the whole the bone seemed fairly mature, indicating that bone deposition and resorption in this densely sclerotic bone were proceeding very slowly. Bone production had evidently taken place through osteoblastic activity, since only an occasional osteoclast was apparent. The newly formed bone was usually well calcified and deposited in a bizarre manner, but on the whole in many areas the sclerosis was due to densely packed, irregular segments of lamellated bone. Although some sections demonstrated a mosaic type of architecture, there was a striking absence of the marrow fibrosis, osteoclastic resorption, and active bone apposition seen in Paget's disease. The cement lines were numerous, irregular, and thickened, but not as irregular and thick as those in typical Paget's disease.

DISCUSSION

The osseous lesion of the case herein described presents certain distinctive features: a monomelic distribution, absence of symptoms, absence of associated deformity and of alterations in the nonosseous tissues of the involved extremity, normal laboratory findings, roentgenographic evidence of a diffuse osteosclerosis limited almost exclusively to the medullary portions of the involved bones, and histologic evidence of replacement of the normal spongiosa by a compact sclerotic bone of irregular pattern composed of numerous irregular fragments of immature and adult bone.

It may be concluded from the evidence presented that this asymptomatic skeletal lesion was unrelated to the other findings in the patient, *i.e.*, the right sciatic syndrome and the probable subclinical scurvy.

The osseous lesion herein described resembles no skeletal lesion hitherto classified. Ontogenetically, the skeleton of the lower extremity becomes differentiated from the sclerogenous mesenchyme of the hind limb bud, condensation extending proximally and distally to produce the membranous anlage of the pelvic bones, femur, tibia, fibula, tarsal bones, and metatarsophalangeal rays. In this anlage is differentiated the cartilaginous skeleton which, in turn, is replaced by the definitive osseous skeleton. A localized disturbance in the primitive bone-forming mesenchyme of the left hind limb may have been a factor in the etiology of the osseous lesion in this case.

It is necessary to consider and exclude, in the differential diagnosis, certain osseous lesions which bear a variable similarity to the lesion herein described, dependent upon anatomic distribution, roentgen findings, and/or histopathologic features.

Melorheostosis Léri (1).—This skeletal lesion has been denoted by other more or less descriptive terms: hyperostosis encoulée, osteosis eburneizzante monomelica, osteopathia hyperostotica rhizomonomelorheostosis, etc. The lesion consists of a dense cortical hyperostosis, consistently monomelic, the sclerotic process extending as a linear streak, "like a hyperostotic flow," through the bones of one extremity into the tarsal or carpal bones. However, although the medulla may be encroached upon, the primary involvement is cortical and associated with considerable periosteal reaction. Furthermore, there are disturbances in the form and length of the involved bones, disturbed function in the adjacent articulations, and, occasionally,

associated skin changes (scleroderma). A congenital origin is suggested by the appearance of deformities shortly after birth; the lesion has been noted to progress during growth. Only six cases have been biopsied. In general, the osseous lamellæ are closely compacted and show a tendency to a bizarre arrangement. The majority of observers consider marrow fibrosis in the medullary canal a constant finding, and the vascularity normal, although Putti (2) noted extremely vascular bone. The photomicrographs in the case reported by Casuccio (3) are instructive. The cortex is seen to have been completely transformed and replaced by spongy tissue with medullary spaces filled by dense fibrous tissue and abundantly vascularized. More deeply, the spongy bone is replaced by trabeculæ of immature fiber bone, formed apparently by osseous metaplasia, and by dense fibrous tissue with a few vessels and no osteoblasts or osteoclasts.

Paget's Disease of Bone.—Henry L. Jaffe has called attention to the endosteal form of Paget's disease referred to by Pick and described more fully by Stenholm and Christeller. Stenholm (4) described the localization of a lesion, in young patients, to the marrow cavity of tubular bones which became filled with fibrous tissue and immature bone trabeculæ (*marzipanähnlichen Gewebes*). His Case 11, that of a 15-year-old boy, presented changes involving, microscopically, the marrow cavities of the fifth lumbar vertebra, both tibiæ, and the right fibula, and, grossly, also the femur and the tenth thoracic and third lumbar vertebræ. His Case 12, that of a 17-year-old girl, manifested deformity and expansion of the right femur due to the replacement of the marrow cavity by fibrous tissue and immature bone spicules, showing a tendency toward "cystic formation" and marked osteoclastic activity. It is a strong likelihood, in view of our recent knowledge as to the histologic features of Paget's disease, that this lesion is not a form of Paget's disease at all.

Although certain areas of the tibial biopsy specimen in the case reported herein suggested a resemblance to Paget's disease, the cement lines were more regular and not as thick, the mosaic architecture was less distinct, marrow fibrosis and osteoclastic activity were not evident, and the lesion was essentially confined to the medullary portions and endosteal side of the involved bones and not associated with periosteal activity. The mosaic in typical Paget bone develops as a result of a complicated cycle of bone resorption and bone deposition. A distinctive feature is the periosteal proliferation and its replacement by Paget bone, following transformation of the cortex, and endosteal resorption (Jaffe, 5). Jaffe (6) has also described an atypical form of osteosclerosis resembling Paget's disease occurring in a 58-year-old man who died of uremia. Ginzler and Jaffe (7) have further noted evidences of osteosclerosis, both macroscopic and microscopic, in adults with chronic renal insufficiency and only mild parathyroid hyperplasia, and have attributed this osteosclerosis to the chronic acidosis incidental to renal damage.

Osseous Changes in Caisson Disease and in Disorders of Undetermined Etiology.—Kahlstrom, Burton, and Phemister (8) have described the bone changes in caisson disease and in other disorders of undetermined etiology, possibly embolic. In these cases, large calcified areas appear in several bones of more than one extremity and are associated with the presence of secondary articular changes. The microscopic picture is that of massive infarction, with extensive areas of bone necrosis and varying amounts of fibrous-tissue invasion, calcification, and new bone replacement.

Despite the roentgenographic similarity between these osseous lesions and the skeletal changes in the writer's case, their anatomic distribution and histologic features are wholly dissimilar. In the case herein reported, there was no history of exposure to abnormal changes in atmospheric pressure or of previous fracture, nor evidence of cardiac disease.

Multiple Neurofibromatosis.—In this condition, skin, subcutaneous tissue, nerve tissue, and the skeletal system may be involved. Although the osseous lesions

usually appear on the roentgenograms as rarefactions, they may be sclerotic, and a monomelic distribution has been described (Case 6, Brooks and Lehman, 9). The diagnosis in this disease rests upon the histologic features of the fundamental lesion, the neurofibroma. In the writer's case, the possibility of multiple neurofibromatosis had to be excluded in view of the sciatic syndrome on the right side.

Polyostotic Fibrous Dysplasia and Skeletal Enchondromatosis.—Although these skeletal diseases are often generalized or bilateral, they may be monomelic instead.

Polyostotic fibrous dysplasia appears roentgenographically as a rarefying, expanding lesion associated with deformity of the involved bones, and the microscopic picture which it presents of fibrous replacement of the medullary substance at the expense of the cortex, with metaplastic formation of trabeculæ of immature bone and occasional islands of cartilage, is distinctive (Lichtenstein, 10). In young subjects, this lesion may be associated with skin pigmentation and with endocrine dysfunction (Albright *et al.*, 11).

Skeletal enchondromatosis is associated with pronounced shortening and deformity of the affected bones, large enchondromas of the tarsal, carpal, and phalangeal bones, and a distinctive histologic picture of disturbed endochondral bone formation.

These two types of lesions may seem to be present in monomelic form because the lesion in other bones has not been visualized roentgenographically.

Other Osteosclerotic Lesions.—The anatomic distribution of the osseous lesion, the roentgenographic and histologic features, and the laboratory findings serve to exclude such generalized lesions as osteopetrosis, osteopoikilosis, osteosclerosis consequent upon certain blood dyscrasias, and chronic fluoride poisoning, as well as the sclerosing lesions of osteomyelitis and certain malignant diseases of bone, primary and secondary.

CONCLUSIONS

The clinical, roentgenologic, and histologic features of a peculiar osseous lesion, hitherto unclassified, have been presented. This skeletal lesion is asymptomatic and is not associated with deformity or disturbed function. It is monomelic in distribution, and represents a diffuse osteosclerosis of slow progression, characterized by the compact apposition of irregular fragments of immature and mature bone, creating an irregular architecture. The lesion involves the inner cortex, spongiosa, and medullary cavity, but spares the periosteum. Its presence is not associated with any abnormal laboratory findings. Although it may well represent a congenital or developmental disturbance in the primitive osteoblastic mesenchyme of the precursory limb bud, its etiology is not certain. For these reasons the designation "monomelic medullary osteosclerosis of unknown etiology" is suggested.

The writer is indebted to Henry L. Jaffe, M.D., for the use of his laboratories at the Hospital for Joint Diseases, New York City.

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X-RAY TREATMENT OF LEUKEMIAS[1]

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From the Radiation Therapy Service of Bellevue Hospital, Ira I. Kaplan, M.D., Director

IN 1902, Pusey reported the treatment of a case of leukemia with the roentgen ray. Since then the procedure has become recognized as the method of choice and although various technics for treatment have been advocated, generally the ultimate results have not been favorably changed. In different clinics various kilovoltages, filters, distances, and intervals between treatments are employed but the results generally are within the same proportions.

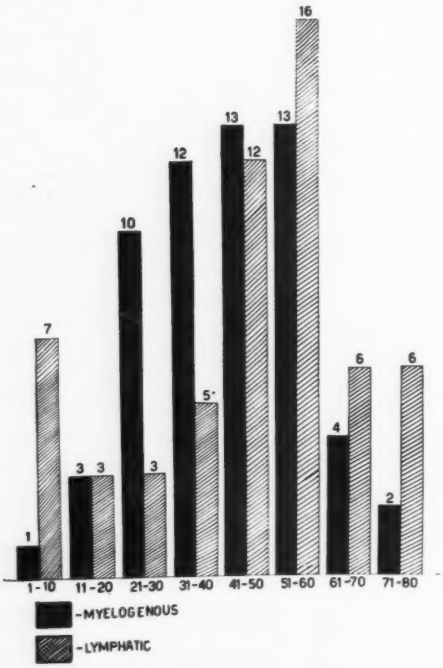


Fig. 1. Age distribution of leukemia.

This presentation does not aim to impress with any startling results in any way at variance from other reports, but includes an analysis of the cases treated in the Radiation Therapy Service at Bellevue Hospital from 1925 through 1938.

[1] Accepted for publication in October, 1939.

Analysis of Cases.—In all, 117 cases are reviewed, 58 of which were of the lymphogenous type, 58 of the myeloid variety, and one of the monocytic form.

Table I reveals the chief complaint as presented in the order of its frequency. Weakness is certainly the dominant symptom in most leukemic patients. Pain is often referred to the left upper quadrant, indicative of splenomegaly. Similarly, swelling of the abdomen, although usually caused by an enlarged spleen, sometimes is the expression of enlarged retroperitoneal or mesenteric lymph nodes.

Figure 1 illustrates graphically the age distribution in both varieties of leukemia. It is seen easily that the frequency in both forms is highest between the ages of 20 and 60 years. Also, lymphatic leukemia is more common than the myeloid type at both extremes of age. In this series, it is evident that nearly 50 per cent of cases of leukemia occurred in individuals from 40 to 60 years of age.

TABLE I

Total number cases leukemia, 117 (lymphatic, 58; myelogenous, 58; monocytic, 1).
Chief complaint (in order of frequency of appearance):

(1) Weakness	(7) Skin rash
(2) Pain	(8) Cough
(3) Enlarged nodes	(9) Anorexia
(4) Swelling of abdomen	(10) Swelling of legs
(5) Dyspnea	(11) Fever
(6) Loss of weight	(12) Vertigo

In Figure 2 is presented the sex distribution. It is obvious that males dominate in the occurrence of this disease, and certainly show a much higher preponderance in the lymphatic type. The actual ratio is 6 to 1 in lymphatic leukemia and 2 to 1 in the myeloid form.

RESPONSE OF BLOOD UNDER X-RADIATION

Myelogenous Leukemia.—Figure 3 represents the response under x-radiation of a

typical case of myelogenous leukemia in which the spleen and ribs were treated. As occurs in most cases when treatment is once instituted, despite the technic or apparatus employed, the total white count fell rapidly. When the decline is persistent and rapid, it will continue even upon the withdrawal of therapy. Based upon such observations it becomes obvious that when a level of from 50,000 to 75,000 white cells has been reached, it is wise to stop therapy. Thereafter, during observation, it will be noted that the count does not rise to the pre-treatment level.

The relationship between the total white cell count, adult segmented neutrophils, and the immature forms is rather constant. When the total count rises, the immature forms become increased, accompanied by a decrease in the adult polymorphonuclear neutrophils. This is expected since there is an outpouring of young forms and a proportional decrease in adult forms. When treatment is instituted and its influence felt, the total count diminishes and the polymorphonuclears show an ascendancy, with a decline in the immature forms. Obviously, such responses are noted only in an individual in the sensitive stage of the disease. It seems, therefore, that when the malady is inactive, there may appear no immature forms in the peripheral blood, although the total white count made largely of adult neutrophils will persist at an elevated level in the neighborhood of from 20,000 to 35,000.

In contrast to the responses of myelogenous leukemia, Figure 4 presents the course of a case of lymphogenous leukemia. It is noted that the lymphocytes, mostly mature forms, persist at an elevated level. The reduction in the total white count actually represents a diminution in the lymphocyte count, but relatively the lymphocytes are in abundance.

Treatment.—Treatments are administered with rays generated at 200 kv., filtered through from 0.5 to 1 mm. Cu and 1 mm. Al, a distance of 40 or 50 cm., giving unit doses of from 150 to 200 r.

The enlarged spleen and ribs were irradiated in myelogenous leukemia. Past experiences have dictated the inefficacy of exposure of the long bones. In lymphoid leukemia, the various lymph node enlargements were treated. If the liver or spleen was enlarged, these organs were similarly treated.

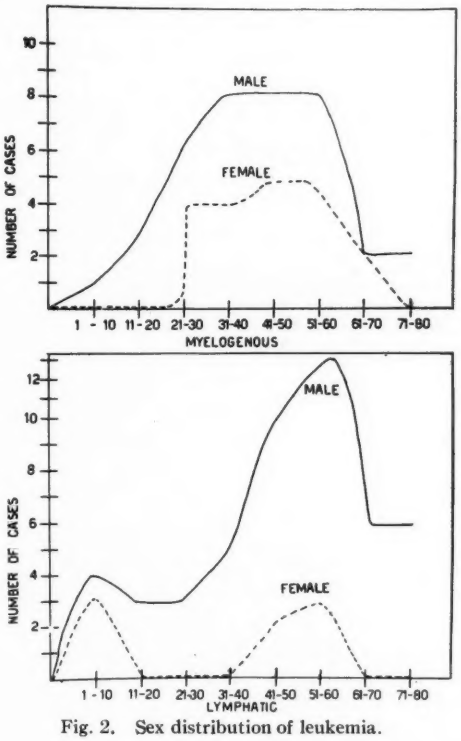
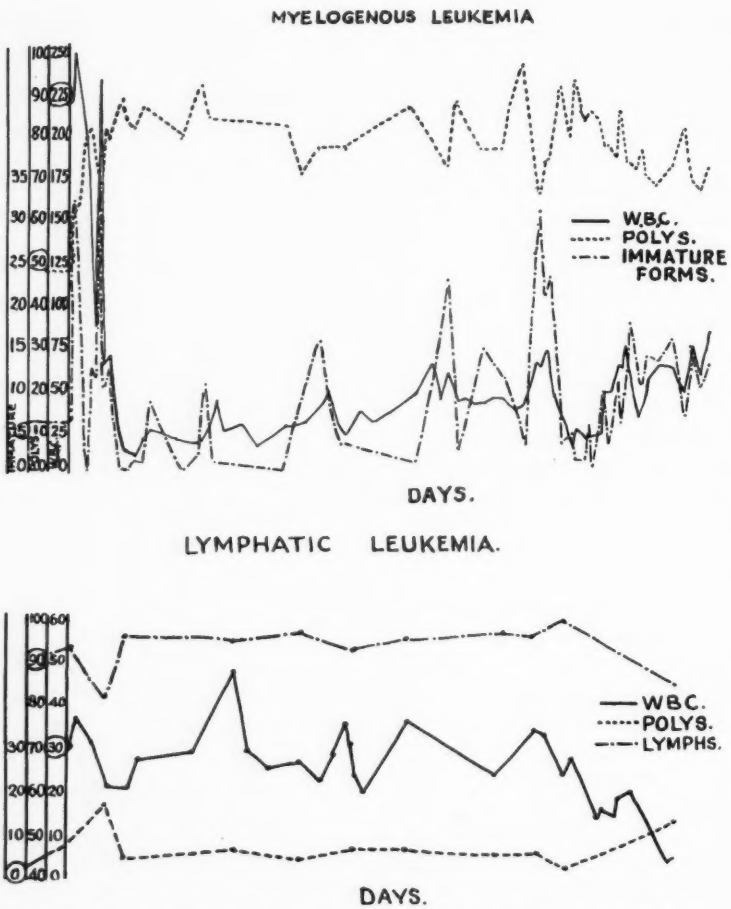


Fig. 2. Sex distribution of leukemia.

As is well known, most cases of chronic leukemia manifest a sensitive response in the early stages of the disease. At some time, however, and with wide variations, there appears a refractory stage, when this standard mode of therapy will produce little effect. It is customary then to alter some of the treatment factors. The filtration is increased, using 1 mm. rather than 0.5 mm. Cu, the distance is increased to 80 cm. to include most of the trunk. The intervals between treatments are decreased and larger unit doses, even to 300 r, are administered. Total body irradiation at 2 or 3 meters or gamma ray or radium therapy may be used. All these are proce-

dures which may be essayed to influence the refractory stage.

Hematologic studies should be done not only to learn the white cell count but to determine the state of the erythrocyte content. Naturally, an anemia should be combated with transfusions and iron therapy. Frequent irradiations will also debilitate the patient and transfusion offers the quickest and most satisfactory tonic. In observing a case of leukemia over a period of years, the level of the white cell count assumes secondary importance with respect to the general condition of the patient. A hematologic examination may reveal a high level of white count, perhaps in the range of from 75,000 to 100,000, yet the individual may present no symptoms. When such condition obtains, it is not unusual for the count to regress spontaneously to a lower level, of perhaps from 25,000 to 50,000, without any alteration in the symptomatology. Therefore, it is the best policy not to treat leukemic patients in the absence of clinical symptoms. The reason for such a stand is justified only on the basis that we may postpone the appearance of the stage at which x-ray is ineffective.



Figs. 3 and 4. Response of myelogenous and lymphatic leukemia to x-radiation.

In the main, our end-results do not differ from those given in previous reports. We have been able to prolong the life span for

a short period, but, unfortunately cannot boast of cures. A statistical analysis of end-results becomes difficult in a city institution like ours because of the nomad tendencies of the economically poor class of patients. However, observing these patients over a number of years has demonstrated that, in many instances, they have been kept alive for periods ranging from three to six years. Furthermore, they have been granted intervals, however long or short, during which they were useful to themselves and the community, when the ordinary day's routine could be normally carried on. Therein lies the great benefit of roentgen-ray therapy.

CALCIFIED MUCOCELE OF THE APPENDIX, WITH RUPTURE[1]

By H. W. OSTRUM, M.D., *and* RUSSEL F. MILLER, M.D., *Philadelphia*

From the Department of Radiology, Philadelphia General Hospital

PRIOR to Virchow's classic description of mucocele, in 1863, when he considered it a "colloid degeneration" of the appendix, Rokitansky, in 1842, described it under the term "hydrops of the appendix." Later, in 1864 and 1888, Cruveilhier and Werth reported the chief complication of the disease as a "gelatinous degeneration of the peritoneum" and as "pseudomyxoma peritonei," respectively. These free and encysted gelatinous masses in the peritoneum, however, are much more common in the female secondary to rupture of pseudomucinous cysts of the ovary and occur only in the male following rupture of a distended mucocele of the appendix. Frankel, in 1901, reported the first case of pseudomyxoma peritonei, with ruptured appendix, containing the same gelatinous substance. Original clinical observations on mucoceles reported by Maydl and Lennander, in 1892 and 1893, respectively, make no mention of autopsy or operative proofs. Numerous case reports by Stengel, Nash, Porter, Deaver, Simon, and others add little to the symptomatology and practically nothing by way of diagnostic criteria. This fact, plus the rarity of this condition, accounts for the low incidence of correct pre-operative diagnosis. Mayo and Fauster, in a review of surgical cases at the Mayo Clinic, 1917 to 1930, inclusive, in 31,200 cases of appendectomy, encountered mucocele of the appendix 76 times—an incidence of 0.24 per cent. Since Virchow's description, approximately 250 cases have been reported.

The clinical diagnosis of mucocele of the appendix is extremely difficult owing to the lack of any constant pathognomonic signs or symptoms. The patient may experience vague abdominal discomfort, pains, and tenderness in the lower right quadrant for many months and not until the pain becomes quite distressing or the tenderness over the appendiceal region markedly intensified is medical relief sought. At this time a palpable tumor mass may be encountered in the lower right quadrant. There may be referred somatic pain or deep splanchnic pain in the region of the appendix, due to tension on the mesentery. Occasionally, as in the recent case of Heatley (1), the patient may present signs and symptoms of an acute surgical condition with fever and leukocytosis as the result of torsion of the proximal appendix incident to rotation of the mucocele; this results in intraluminal and interstitial hemorrhage and gangrene.

The use of x-ray in investigation of mucocele of the appendix has been considered limited, due to the fact that the proximal lumen of the appendix is almost invariably completely stenosed, thus prohibiting the entrance of any of the opaque medium; also, because of failure to elicit signs of extrinsic pressure on the barium-filled cecum. Rarely is there patency of the proximal end to permit passage of the barium and allow for full visualization of the entire mucocele, as in the case reported by Vorhaus. Incidentally, the latter's case also showed irregularity of the lower portion of the cecum, produced by changes similar to those found in the appendix. He also noted the intermittent regression and exacerbation of the mass when stenosis of the lumen subsided, followed by complete collapse of the tumor, with a re-filling at some later date. This patency and entrance of bacteria somewhat modify the conception of the development of this condition, which usually results in complete stenosis with sterile contents; other-

[1] Accepted for publication in October, 1939.

wise empyema or gangrene would result. This fact leads one to believe that mucocele may be produced not only by inflammatory obliteration of the proximal portion of the lumen of the appendix through partial or total destruction of the mucosa or by post-inflammatory adhesions, but also by mechanical interference with the filling and emptying of the appendix.

Wangensteen and his associates were able to collect from 1 to 2 c.c. of secreted fluid daily from the tip of a normal unobstructed appendix. They also demonstrated that the volume of the lumen was small and, under normal conditions, varied from 0.07 to 1.4 c.c., depending upon the pressure of the contained fluid. This small volume seems important when considered in relation to the quantity of secretion that might be formed under normal and abnormal conditions, accompanied by interference with the emptying mechanism of the appendix through the synchronous contraction of its circular and longitudinal muscle layers, originating in the tip and moving toward the cecum. These writers also present evidence in favor of functional stasis by demonstrating a resistance to luminal flow during perfusion of the appendix, both *in situ* and after removal. In studying the muscle layers at the junction of cecum and appendix in 250 appendices, they found that 59 per cent showed thickening of the circular muscle on the medial aspect of the superior wall; although there was at no time any evidence of a circular sphincter, it had sphincteric-like action. Westphal and Schmidtlein demonstrated in the human, by means of x-ray, the sphincter-like action of the proximal third of the appendix following stimulation of smooth muscle by the intravenous injection of pilocarpine.

Whether stagnation (other than that brought about by chronic obliterative appendicitis) due to stricture, adhesions, congenital membranes, kinks, fecaliths, foreign bodies, functional stasis, etc., plays a part in the production of mucocele is, of course, conjectural. The fact that a mucocele retaining its opening with the cecum has been reported would lend support to the idea that it need not necessarily be of inflammatory origin with atresia of the lumen, for Gerlach's valve, which is a fold overlying the appendiceal orifice, is believed to interfere with or preclude the filling of the lumen of the appendix. Its absence, which is frequent, would facilitate obstruction of the appendix with consequent inflammatory reactions.

Wangensteen found that human appendices which were not obstructed had a luminal capacity, at 20 cm. of water pressure, of only 0.23 c.c.; at 60 cm. water pressure, the highest luminal capacity was 0.7 c.c. On attempts to break the normal appendix by increasing the pressure, it was found that none of the appendices, directly following excision, could be ruptured by pressure as high as 2,400 cm. of water. The presence of an inflammatory reaction in the appendiceal wall greatly decreases its strength. Unruptured, gangrenous appendices break at very low pressures. All varieties of appendicitis recognized by pathologists may be produced by luminal obstruction in animals whose vermiform appendix possesses the capacity to secrete fluid as does that of man. The vermiform appendage of the rabbit will perforate quite regularly after from 10 to 14 hours of obstruction. Fecaliths and swelling of lymphoid tissue are probably the most frequent causes of appendiceal obstructions in man, although kinks, bands, position (retrocecal) and stenoses may also cause obstruction.

Most observers believe that chronic obliterative appendicitis follows an acute attack and is not the end-result of a process of physiologic atrophy. Those portions of the appendix in which there is complete destruction of the mucosa become adherent and eventually fuse; this might involve the appendix as a whole or in part. When the proximal lumen is obliterated, distention by mucus secreted by active mucous glands, results in the formation of a mucocele. With an increase of tension within the mucocele, there is an accompanying pressure atrophy of the mucous membrane;

this apparently alters the character of its secretions, *i.e.*, mucin is transformed into psuedomucin, identified chemically by Hammarsten, who later demonstrated a reducing substance isolated by Zängerle as "glucosamine." Later, due to complete atrophy and cessation of secretion by mucous glands, nothing but a thin, watery cyst remains. This may be the result of interchange of fluids along with seepage of and hemorrhage; rupture with the production of psuedomyxoma peritonei is the gravest complication, for the latter is potentially malignant. However, this may not occur in cases in which there is pressure atrophy of the lining mucous membrane; here the cyst wall is thin and the contents watery. Also, as in the case herein presented, rupture does not necessarily have to occur intraperitoneally.

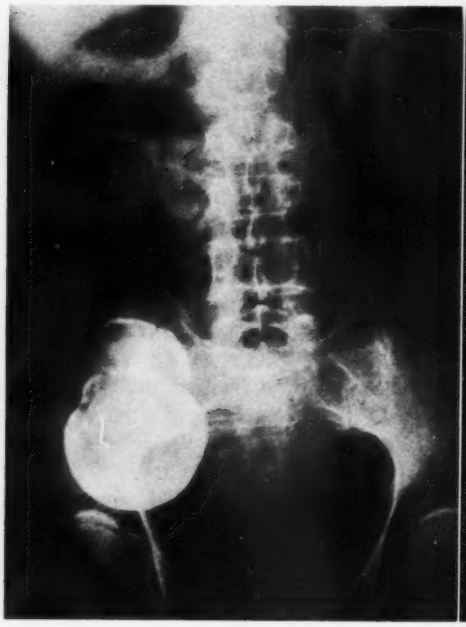


Fig. 1.

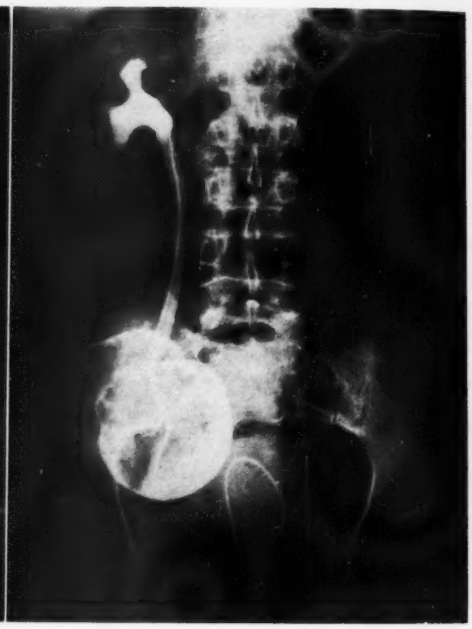


Fig. 2.

Fig. 1. Plain film showing the large, dense annular shadow of the mucocele connected by a broad isthmus to a smaller sac along its superior border; the edges are smooth and regular in outline while irregular plaques dot the interior.

Fig. 2. Ureteropyelogram of the right side, showing a ureterectasis and mild degree of pyelectasis. Note the pressure effect of the mucocele on the lower portion of the ureter.

lymph from neighboring mechanically engorged blood vessels. Most of these cases are diagnosed as acute or chronic appendicitis, retroperitoneal neoplasm, carcinoma of cecum, ovarian cyst or dermoid, intestinal obstruction, intussusception, uterine fibroids, terminal ileitis, ectopic kidney, etc.

Mucocele occurs most frequently in middle life or later, although Heatley's patient was a girl 16 years of age. The complicating factors include herniation into the cecum (2), torsion with gangrene,

CASE HISTORY

J. K., white male, 73 years of age, was admitted to hospital twice, first from March 9 to March 28, 1936, and the final admission on Aug. 29, 1938. The patient died on Sept. 5, 1938. His chief complaints upon first admission were difficulty in moving his arms and legs and generalized weakness. Upon x-ray examination a large, irregular calcified tumor mass, freely movable, not connected with the right kidney or ureter, producing a pressure

defect on the cecum, but with no intrinsic involvement of the latter, was found in the right lower quadrant. On the second admission there was a greater amount of weight loss. Constipation was a predominating symptom during the first week, later changing to a diarrhea which was bloody at times. Upon rectal examination, the tumor mass was found to be harder than upon the previous examination, situated somewhat lower, and more tender to palpation. The patient became weaker, and complained of pain and tenderness in the abdomen. He ran a low-grade fever.

Fig. 3.

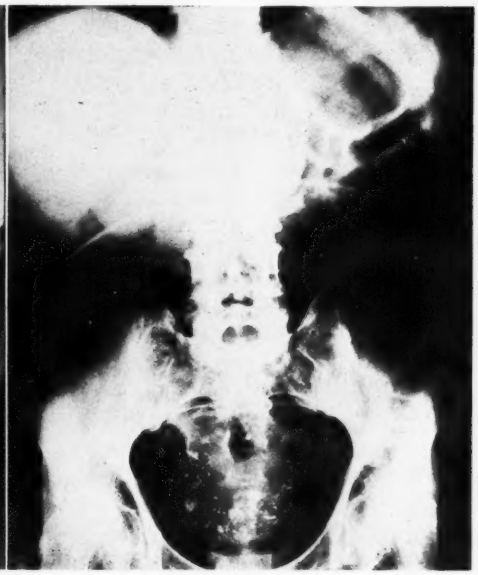


Fig. 4.

Fig. 3. Barium enema study showing "flattening" of the inferior margin of the cecum; a pronounced upward convexity was produced by cephalad displacement of the mucocele.

Fig. 4. A film made after the disappearance of the palpable mass, showing what remains of the calcium débris following rupture. Practically all of the débris lies within the lumen of the bladder.

At autopsy the heart showed aortic calcification, ulcerative atherosclerosis, myocardial fibrosis, and coronary arteriosclerosis; the lungs showed emphysema, passive congestion, and bronchopneumonia. The kidneys showed severe toxic nephrosis and the gastro-intestinal tract revealed a calcified mucocele of the appendix with vesical-rectal-sigmoidal and ileal fistulæ; also, chronic ileitis and chronic nonspastic colitis. The liver showed passive congestion and parenchymatous degeneration. The collapsed cyst, occupying the pelvic basin, when opened measured 10 × 10 cm., being partly filled with a gray gelatinous mucoid, semi-fluid material clinging tenaciously to the firm gray-white fibrous wall. No remnant of the appendix could be found. Of the five connecting fistulæ, the oldest appearing one was found to be along the mesial border of the cecum, measuring approximately 4 cm. in diameter, its edges rounded and smooth. A solitary nodule, consisting of the same gelatinous material as the mucocele, projected through this orifice into the lumen of the cecum. A similar but smaller fistula entered the rectum 3 cm. above the prostate level, while the third fistula, approximately 1 cm. in diameter, opened into the lateral aspect of

the bladder; the fourth entered the sigmoid 5 cm. above the rectosigmoid junction, and the fifth entered the terminal ileum 5 cm. above the ileocecal valve; here the mucosa was swollen, and of a dirty brown color, associated with a reddish and ulcerated plica circularis. The entire colon was thickened, boggy in character, with grayish discoloration and reddish-purple granulations, and redundant mucosa. The bladder wall was also swollen, discolored, and showed numerous areas of superficial ulceration.

The final diagnosis was calcified mucocele of appendix, with fistula into rectum, sigmoid, cecum, ileum, and bladder.

SUMMARY

1. The presence of an open passageway between the cecum and mucocele of the appendix to allow the entrance of barium into the latter, readily establishes the diagnosis. This patency, however, is rarely encountered and only one case has been reported as such. Again, an empty or at least partially empty sac at the time of the examination would be necessary to its demonstration, for a distended mucocele would prohibit further entrance of any fluid, thus obviating any direct visualization.

2. Indirect signs of the presence of a mucocele can be elicited during fluoroscopic examination by palpation of the lower right quadrant, with pressure directed toward the cecum. The displacement of the mucocele in this manner will produce a smooth filling defect along the mesial and inferior border of the cecum. Palpation must be done with care, so as to avoid possible rupture of an atrophic and thin-walled sac. If the mucocele is fixed by adhesions close to the border of the cecum, an alteration in its outline can be seen fluoroscopically to occur in rhythm with respiration. This is due to the abuttment of the cecum against a relatively fixed object, brought about by diaphragmatic action and corresponds to partial emptying of the cecum in deep inspiration and refilling in the expiratory phase.

3. In addition to extrinsic pressure defects, the barium-filled coils of terminal ileum might be sufficiently displaced to describe an arc, indicating the presence of an intraperitoneal mass.

4. In the male, the presence of a clear-cut, dense, intact annular shadow in the lower right quadrant, the walls of which are smooth and regular, while within their confines are numerous irregular, closely arranged plaques, is strongly suggestive of mucocele.

5. Mucoceles are practically always unilocular, though there may be a gradual narrowing and tapering along the border adjacent to the cecum presenting a pear-shaped shadow. The smooth, rounded border readily differentiates it from other dense shadows in this region such as calcified ovary or uterine fibroid. These are more apt to appear as irregular collections of punctate shadows of varied size within a fairly well defined but rough and uneven border. The latter are often multicentric.

6. Teratomas and dermoid cysts occurring in the ovary frequently contain bone and cartilage with calcium deposits, and the enamel structure of a tooth, if present, produces an unmistakable shadow. Here again, the wall is irregular and often incomplete and the shadow as a whole is heterogeneous in character. While Kaufman reports calcium deposits in chronic ovarian and tubular abscesses in the interstitial tissue of carcinoma of the ovary, and the presence of psammoma bodies (small granular structures composed of calcium carbonate) in the papillæ and cyst walls of papillary cystadenomas, we have never demonstrated any of these densities *in vivo* by x-ray examination, although with soft-tissue technic we have shown irregular groups of fine granular deposits in carcinoma of the ovary removed at autopsy. It seems unlikely, however, that sufficient calcium exists, in the majority of cases, to cast recognizable shadows on routine films of the abdomen.

This case is unique in that (1) we believe it to be the first case of calcified mucocele of the appendix reported; (2)

we have demonstrated collapse of the tumor with emptying of its contents into adjacent hollow viscera.

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OSTEOCHONDRODYSTROPHY (MORQUIO)[1]

CASE REPORTS AND FOLLOW-UP

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MORQUIO (1), in 1929, described two cases of an unusual clinical picture of familial chondrodystrophy. In 1935, he supplemented his original treatise with reports of two more brothers in the same family of five, who had become affected with the same syndrome. He gave a graphic report of the skeletal deformities involving all the epiphyses and especially the weight-bearing joints. He described fully the roentgenograms and discussed the etiology.

Since that time, some 30 cases have appeared in the literature. Ruggles (2), in 1931, described the clinical and roentgen findings in eight cases of a peculiar type of dwarfism which he had followed since 1918, all of which bore a striking resemblance to those described by Morquio. Meyer and Brennemann (3), in 1932, discussed in a detailed case report, a clinical picture which resembled closely Morquio's cases. Subsequently, Coward and Nemir (4), Barnett (5), Brown (6), and others have presented reports describing the condition. Freeman (7), in 1938, presented a critical review of the literature and reported one case, presenting the same clinical picture as described by Morquio, that is, dwarfism, kyphosis, genu valgum, pes planus, and muscular flabbiness. However, there was no evidence of a familial tendency. Jacobsen (8), in 1939, reported an interesting family in which 20 members of five generations were affected.

As yet, there is little known regarding the true etiology of the disease. Morquio's patients were from consanguineous parents and some observers were wont to attach significance to this factor. Morquio also reported low calcium levels to which he attributed this disturbance in bone development. This, however, has not been borne out in subsequent reports and was not present in our patients. Morquio also suggested that some endocrine or metabolic disturbance might play a rôle in the defective osteogenesis, but results thus far fail to substantiate this idea.

Giraud and Bert (9) advanced the theory that the disease was primarily an arthro-ligamentary dystrophy and thought that the weakness of the ligaments might lead to weakened skeletal resistance, which, in turn, under the influence of the upright position, might result in luxations and permanent deformities. This explanation, however, does not adequately account for the changes. Indeed, there is nothing definite to date to explain all the widespread osseous deformities and the characteristic changes in the epiphyses of the long bones.

CASE REPORTS

Case 1. C. C. (History No. 3,654.) White boy, aged five years, was first seen in March, 1931, by the Orthopedic Department. The complaint was "dislocated hips, knees, and ankles" since the age of one. The patient appeared normal at birth and seemed to develop normally until he tried to walk, at which time the parents noted that he could make little progress. The father stated that, "the child's feet and legs seemed chunky and soft and his bones seemed poor." The family history was negative except that one sister, a year older than the patient, had a similar condition. Four children born since were apparently normal.

Examination at this time showed the boy to be well nourished and mentally

[1] Accepted for publication in July, 1940.

alert. The dorsolumbar spine showed slight kyphos and there were bilateral dislocation of the hips, 45-degree genu valgum deformities, and unstable flat feet. The child could not support his body weight except with crutches. The muscles showed no atrophy but were flabby. The remainder of the physical examination was negative and the laboratory studies were normal. Roentgen-ray studies showed bilateral dislocation of the hips. The epiphyses of the femoral heads had not appeared and both acetabula were quite shallow (Fig. 1). There was retarded development of all the carpal and tarsal bones, and the epiphyses of the metacarpals and metatarsals were just beginning to appear (Figs. 2-*A* and 2-*B*). There were flattening and broadening of the distal diaphyses of the long bones, particularly of the femora. The epiphyses were also very ragged and of irregular density (Fig. 3).

The patient was seen on numerous occasions during the years 1931–1935. The deformities gradually grew more marked and the muscles of the extremities were underdeveloped, but he used his crutches fairly effectively. He seemed quite susceptible to upper respiratory infections and colds, which interfered with his general well-being.

In February, 1936, he entered the hospital complaining of anorexia, epigastric pain, nausea and vomiting spells, and questionable history of tarry stools. He was investigated from the standpoint of a bleeding peptic ulcer, but laboratory and roentgen studies failed to confirm the diagnosis. The red blood cell count was 4,000,000, hemoglobin was 70 per cent, white cell count was 16,000. Urine was negative. The tuberculin and Schick tests were negative. The patient improved on a Sippy régime and was discharged. At this visit, the deformities were more pronounced, particularly the kyphoscoliosis.

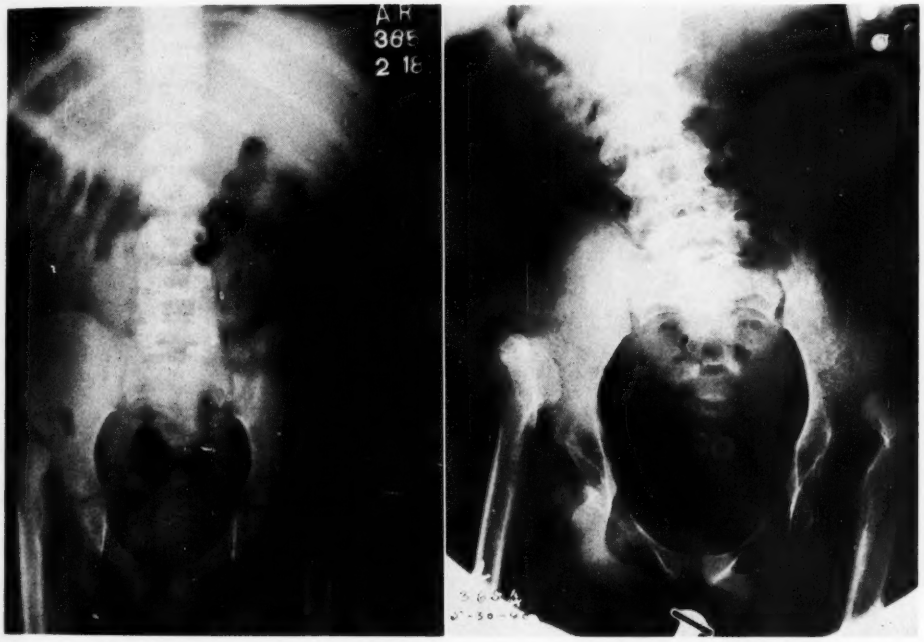

Fig. 1. Roentgenograms showing bilateral dislocation of hips and delayed appearance of the epiphyses. Note development of kyphoscoliosis.

In 1937, the boy reappeared complaining of difficulty in swallowing, and vomiting. Roentgen studies showed evidence of an esophageal stricture or possibly an anatomic short esophagus, and numerous subsequent studies showed gradual increase in the stricture, with eventual protrusion of the stomach into the left thorax. Under care for dilatation of the stricture the symptoms improved.

Throughout the course, the laboratory studies have remained normal, with no demonstrable changes in the calcium, phosphorus, and phosphatase.

At the present time, the skeletal deformities are quite marked and the thorax is distorted by the extreme kyphoscoliosis. Roentgen-ray studies in April, 1940, showed bone growth but all the epiphyses were retarded. There was considerable increase in kyphoscoliosis.

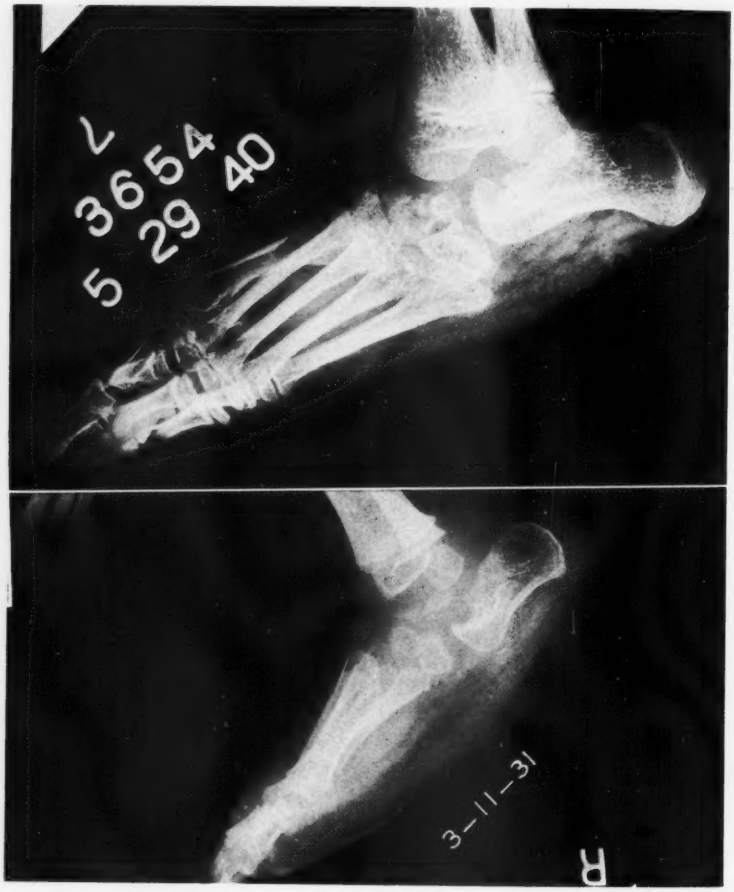

Fig. 2-*A*. Plates showing retarded development of the tarsal epiphyses at age of five and fourteen.

Case 2. The sister, aged six years, presented an almost identical pathologic process and the findings were consistent with those described by Morquio.

CONCLUSIONS

Two cases, in a brother and sister, are presented which conform to the clinical syndrome first described by Morquio.

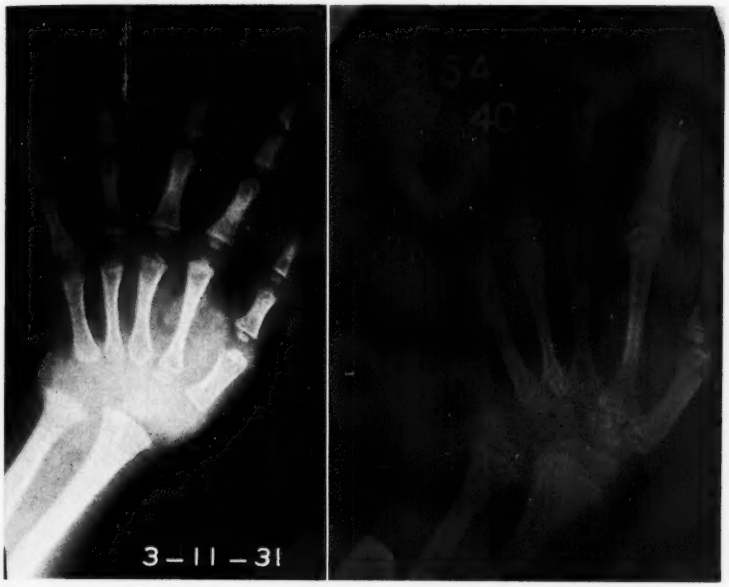

Fig. 2-*B*. Changes in the carpal regions similar to those in the tarsus (Fig. 2-*A*)

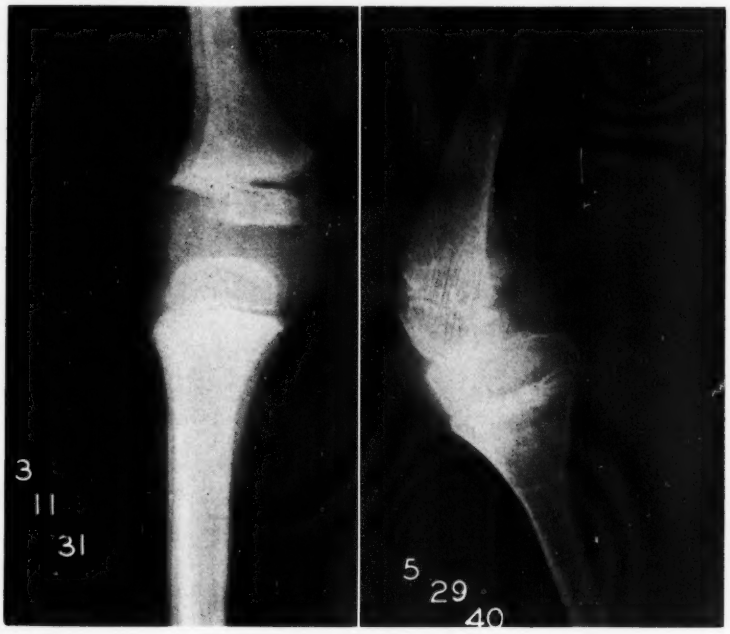

Fig. 3. Roentgenograms showing the knee joint at the age of five and fourteen years. Note the ragged epiphyses and broadened diaphyseal lines; also, deformity.

The syndrome presents a characteristic roentgen picture, delayed epiphyseal growth, ragged, flattened diaphyseal lines, delay in appearance of the carpal and tarsal bones, flattening of the vertebral bodies, resulting in kyphoscoliosis, and marked symmetrical deformities of the joints.

The cases do show familial tendency.

No disturbances in the calcium phosphorus metabolism were present to account for the syndrome.

Our two cases, with follow-up examinations and the roentgenograms, are presented with a view of stimulating more thought as to the cause of this generalized deficiency in cartilage growth.

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CASE REPORTS

MULTIPLE MILIARY CALCIFICATIONS IN THE LUNG[1,2]

By ANTONIO MAYORAL, M.D., *New Orleans, Louisiana*

In roentgenologic practice one occasionally finds in roentgenograms of the thorax of individuals who present no symptoms, or whose history does not suggest past serious illness, multiple scattered shot-like calcifications throughout the lung-fields. The mental reaction to such roentgenograms is "healed miliary tuberculosis."

Caution, however, must be exercised before accepting all of these as cases of healed miliary tuberculosis. The work of Sayers and Meriwether (1) has brought to light a number of persons presenting generalized symmetrical calcifications in the lungs, presumably of non-tuberculous origin. These authors have set forth convincing evidence toward the mycotic origin of the condition and believe the *Aspergillus niger* to be the pathologic fungus. Sutherland (2) reports a series of cases presenting similar x-ray findings in which it is highly doubtful that tuberculosis is the cause; while Virchow (3), as early as 1855, called attention to calcium deposits in the lungs of persons who were suffering from extreme caries of bone, or some other bone destructive condition, and called the deposits "calcium metastasis." Granting that tuberculosis is not the cause of all miliary calcifications in the lung, the fact remains that it is the cause of at least a large majority.

The clinical conception that miliary tuberculosis is a disease necessarily fatal, and rapidly so, has become unsustainable in view of roentgenologic explorations of the chest revealing lungs showing miliary seeding in patients who have outlived the expected early death from miliary tuberculosis and others who, in apparently perfect health, show shot-like calcifications within the lungs not unlike tuberculosis of the miliary type.

The first cases reported as healed miliary tuberculosis were diagnosed solely on the findings of miliary calcifications on x-ray films, and accepted as such, with little or no pathologic background (4, 5, 6). In these early cases, apparently no attempt was made to differentiate between hematogenous and bronchogenous spread of infection or to investigate the etiology. If a series of roentgenograms showing the condition described by Sayers and Meriwether (1) and Sutherland (2) are compared with roentgenograms of what is accepted to be healed miliary tuberculosis, and the literature carefully scrutinized, one is forced to admit that no satisfactory criterion for differential roentgenologic diagnosis has been offered, and that no one has presented conclusive and convincing evidence acceptable in making the differential clinical diagnosis of the calcifications in question. Reviewing the literature one also gets the impression that the healed miliary tubercle being discussed herein is the end-result of the acute tubercle of acute miliary tuberculosis. It is difficult, however, for anyone who has seen clinical acute miliary tuberculosis to accept this conception *prima facie*.

The above statement needs further clarification and to illustrate what is meant, three cases, one chronic, one acute, believed to follow hematogenous spread, and a third believed to be of bronchogenous spread, will be presented and discussed.

Case 1. A patient brought me a film (Fig. 1) sent by a former technician who knew me to be interested in lungs, presenting roentgenologic evidence of miliary calcification. The patient assured me that he was at present in excellent health, having been engaged during the past ten years in very strenuous work, with no subjective physical deterioration. To his knowledge he had never been seriously ill and had suffered only minor ailments. The calcifications seen in the roentgenogram had been found accidentally several years before. A study of this roentgenogram shows numerous calcifications well scattered throughout both lungs, of a striking uniformity of size, density, and distribution; a typical case of healed miliary tuberculosis of the lung.

Case 2. Shortly before the above patient consulted me, a young male Filipino had been admitted to the hospital seriously ill, with a high fever of undetermined origin. He had worked up to the day of his illness, that is, two days before admission. Two days following admission, a roentgenogram of the chest was made (Fig. 2); the diagnosis was acute miliary tuberculosis. The patient died four weeks after the onset of illness. Autopsy confirmed the diagnosis.

To prove that the condition found in the chest of the first patient is the "burnt-out" terminal stage—as compared with the calcified soft nodules seen in the chest of the second patient—would be simple had it been possible to follow with a series of roentgenograms the acute tubercle through different stages of fibrosis and final calcification, or if the tubercle bacillus had been found within the calcified

[1] Accepted for publication in May, 1939.

[2] Published with the permission of the Surgeon-General of the United States Public Health Service.

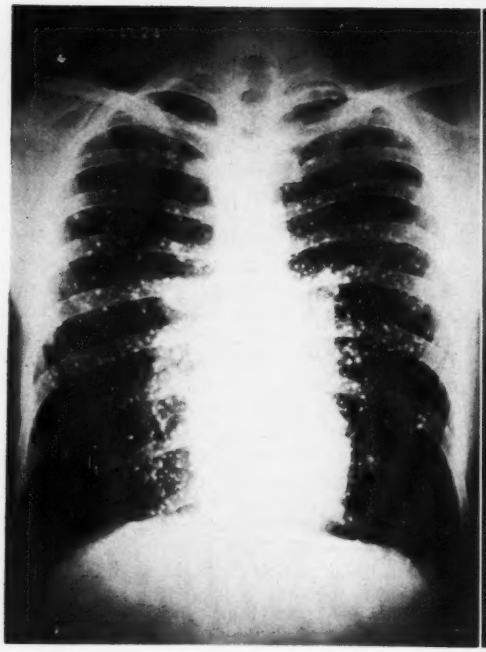

Fig. 1. Case 1: Healed miliary tuberculosis. The patient's history was negative and the miliary calcifications were an accidental finding.

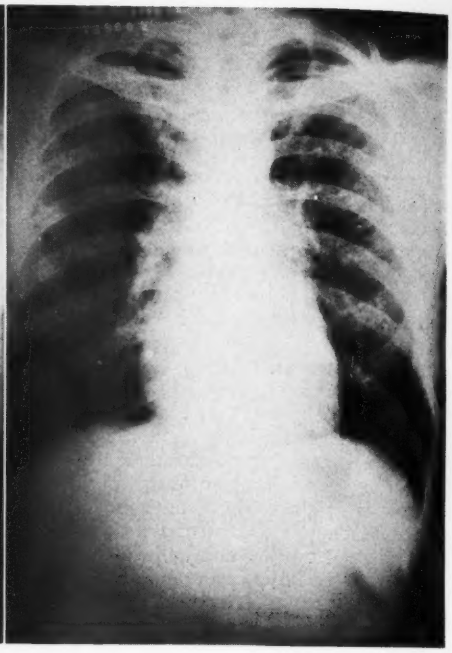

Fig. 2. Case 2: Acute miliary tuberculosis. This patient was admitted to the hospital acutely ill and died within four weeks.

nodules (7); but this, as far as I know, has not been done. Studies by Opie and Aronson (7), however, indicate that demonstrable tubercle bacilli are not derived from these caseous or calcified nodules but are contained in the tissue surrounding them. This seems sufficient circumstantial evidence to pronounce the tubercle bacillus at least guilty.

The diagnosis of healed miliary tuberculosis in our first patient, based on this circumstantial evidence, seems, therefore, acceptable.

The etiology of the second case is clear. If, as I believe, the tubercle bacillus is responsible for the findings in both lungs, why the difference in symptomatology, course, and final outcome in the two patients?

It is a well known fact that in primary infections invasion by a tremendous number of tubercle bacilli is tolerated with little or no clinical manifestation (9). It is generally accepted that from three to seven weeks are necessary for tissue to become sensitized to the bacillus (9), and experimental pathology has shown that the growth of the bacillus is rapid and multiplication begins early when it finds its way into the blood stream (8). Based on the above facts, two hypotheses are offered as answer to the question, as follows:

(*A*) During first-infection type of tuberculosis, the bacillus is carried by the lymph vessels from the point of entry to the nearest lymph nodes, where the first line of resistance is met. This constitutes the primary complex and usually ends there, but no one has demonstrated that the bacillus cannot travel beyond this first line of resistance and by way of the efferent lymph vessels, the thoracic duct, and vena cava reach the lesser circulation and seed the lungs with multiple foci before sensitization, at a time when the individual resists the infection without clinical manifestation.

(*B*) Endogenous seeding from an old dormant lesion which has been inactive long enough for the tissues to become desensitized and has suddenly become active, discharging its contents into a blood vessel or the thoracic duct, may occur.

The discrepancy in the clinical findings between these two cases is due to the state of the tissues at the time of infection; that is, if the infection takes place in a sensitized individual it presents the clinical entity of acute miliary tuberculosis, but if the bacillus is seeded in less sensitized lung tissue it may proceed to cause the same pathologic entity but without clinical manifestations.

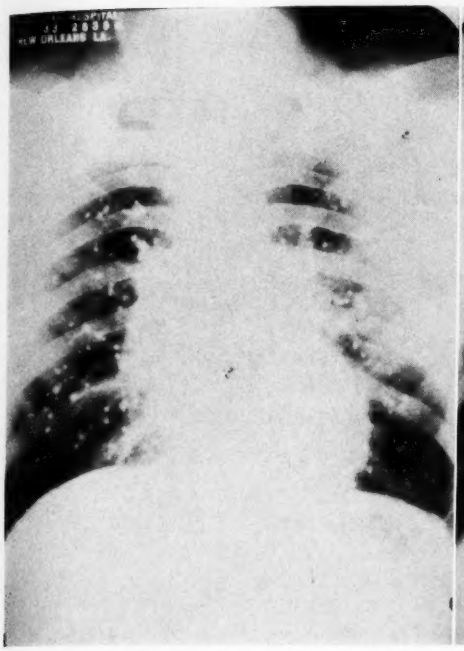

Fig. 3. Calcified tubercles, product of bronchogenic spread, a common finding in routine chest examinations of healthy persons.

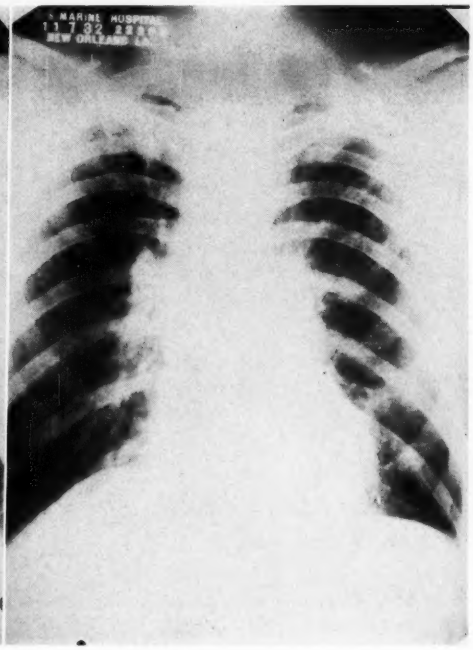

Fig. 4-*A*. Case 3: Tuberculous lesion at right apex in a patient with a two-year history of chest symptoms.

In an effort to diagnose early tuberculosis, school boards and health departments are carrying out an active campaign among school children and many roentgenograms of the chest are being made. The confirmation of the hypothesis set forth in this brief paper might be found among these children, as it is during childhood that most primary infections occur. Many thousands of chest roentgenograms, however, must be available for this investigation, as multiple seeding of the lung as a primary complex appears to be rare and because, judging from observations of tuberculosis in general, the regression of many of these tubercles before the calcified state is reached should be expected. The lesion to look for is the well known mottling of acute miliary tuberculosis, which, if found, should be followed by serial roentgenograms. I believe, however, that the confirmation of the hypothesis would be easier if the investigation were extended to infants, since by the time children are of school age, calcification has probably already taken place.

In the preceding discussion, healed miliary tuberculosis is believed to be the product of hematogenous seeding. Let me emphasize certain roentgenologic characteristics of these calcifications: first, their striking uniformity in size; second, they are all of about the same density, suggesting that they are all of the same or nearly the same age, and, last, their symmetrical bilateral distribution. The lung-fields present no other demonstrable pathology. The patients are in apparent perfect health and give no history of serious illness.

In contrast to the preceding cases, chests presenting multiple calcified nodules, very irregular in size and distribution and density of individual nodu'es (Fig. 3), are found quite commonly in routine examinations of apparently healthy individuals. However, when the patients are thoroughly questioned, a history of old tuberculosis or typhoid pneumonia or long-drawn-out colds, pointing toward an unrecognized tuberculosis, is found and quite often these fibrous lesions and contractions of the apex can be seen in the chest roentgenograms as evidence of old healed pulmonary tuberculosis. These calcified tubercles are the product of bronchogenic spread, and are, in reality, calcified patches of tubercular bronchopneumonia. To illustrate, a typical case is presented.

Case 3.—H. F., 38-year-old white seaman, was admitted to the hospital on Aug. 15, 1931. The diagnosis was pulmonary tubercu-

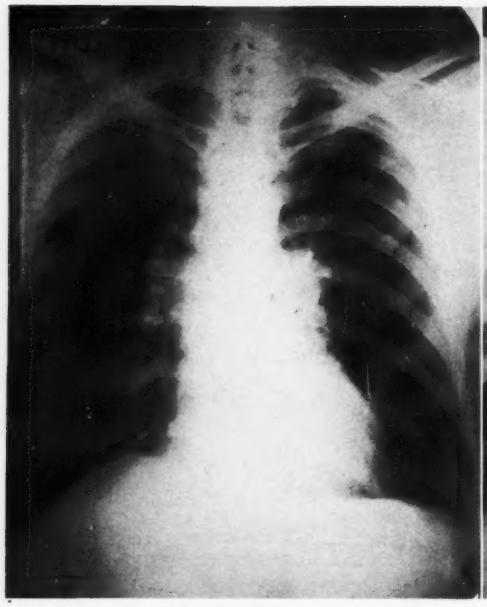

Fig. 4-*B*. Case 3: Dissemination of lesions through right lung. Roentgenogram made a year and ten months after Fig. 4-*A*.

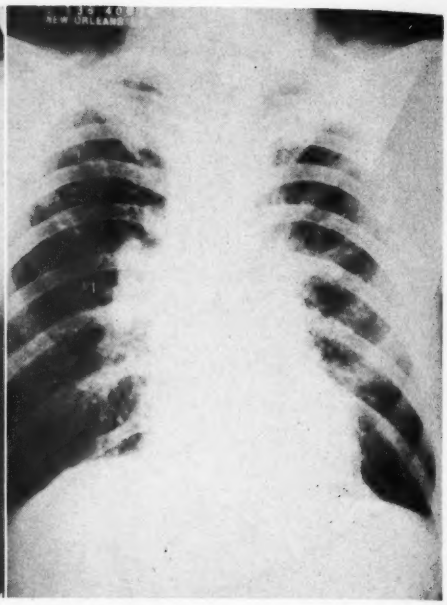

Fig. 4-*C*. Case 3: Calcification of some tubercles; increased dissemination in both lungs, two years and three months later.

losis. Previous history revealed that for two years before admission the patient had been annoyed by intermittent pains in the chest. Lately they had become very acute and eighteen days before admission he had developed a severe productive cough. The patient requested hospitalization because of progressive weakness. Physical examination revealed signs of active lung involvement, which proved by laboratory and roentgenologic findings to be tuberculosis. He has remained under our observation as an in- or out-patient for the past five years. During this period toxic symptoms have been minimal, but local chest signs and symptoms have been always prominent. Roentgenologic lung studies on admission (Fig. 4-*A*) revealed a minimal tuberculous lesion at the right apex. One year and ten months later (Fig. 4-*B*), scattered soft disseminations were visible throughout the right lung. The next film (Fig. 4-*C*), taken two years and three months later, shows calcifications of some of the soft tubercles seen in previous films and a greater dissemination throughout both lungs. The patient is at present working and in apparently excellent health. The final diagnosis was healed miliary disseminated tuberculous bronchopneumonia.

Conclusion.—When roentgenologists demonstrated multiple shot-like calcifications in the lung-fields, healed miliary tuberculosis became an acceptable clinical diagnosis. For those who have seen cases of acute miliary tuberculosis, it is difficult to accept the fact that the healed variety is a terminal stage of this acute disease, which is the impression gained by reviewing the literature.

Pioneer pathologists studying the behavior of the tubercle bacillus during primary and secondary infections have furnished information for formulation of acceptable hypotheses to explain the healed stage of acute miliary tuberculosis. When seeding takes place in a desensitized individual and, therefore, at a time when tissue is highly tolerant to the infection and he offers no outward manifestation of the disease, the tubercle may form and proceed to calcification, being discovered accidentally years later, the patient being unaware of having once been afflicted with tuberculosis.

It is possible, by careful study of the roentgenograms, to make a differential diagnosis between healed acute miliary tuberculosis and healed miliary disseminated tuberculous bronchopneumonia. I repeat: in healed miliary tuberculosis the history is negative, the chest films show numerous scattered calcified nodules of symmetrical bilateral distribution of striking uniformity in size and of equal density, the lung parenchyma being otherwise clear.

In healed miliary disseminated tuberculous bronchopneumonia, there may be a clearly unmistakable history of previous tuberculosis or one quite suggestive of the condition. The nodules are irregular in distribution, shape, and size and are found in all stages of calcification. Scrutiny of the roentgenogram will reveal old signs of healed tuberculosis usually in the upper lobes or retraction of one or both of the apices.

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GASTRIC SYPHILIS[1]

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From the Department of Radiology, Duke Hospital and Duke University School of Medicine

Golob has recently written a comprehensive review of gastric syphilis. In his paper he included the Carman-Eustermann criteria for syphilis of the stomach. We quote only the roentgenologic portion.

(1) Filling defect of gastric outline, usually without corresponding palpable mass.
(2) Hour-glass stomach (dumbbell) of the upper loculus may be tubular, owing to extensive irregular concentric contraction.
(3) Six-hour retention less frequent than in other gastric lesions (about 20 per cent).
(4) Diminution of gastric capacity.
(5) Stiffening or lessened pliability of the gastric wall.
(6) Absence of peristalsis from involved area.
(7) Pylorus free rather than obstructed.
(8) Patient not ill proportionate to the extent of the disease shown by the x-ray examination.
(9) Absence of niche, accessory pocket, or typical incisura; classical signs of simple gastric ulcer (1).

From Moore and Aurelius (2) we find that of 87 cases of gastric syphilis 70 per cent were prepyloric; 22 per cent were median; and 8 per cent were diffuse.

Case Report.—J. W. (Case No. 70,749), a 39-year-old colored male, first seen in our outpatient department, was admitted to Duke Hospital on Feb. 28, 1938, complaining of nausea and vomiting for the past eight months. The vomiting usually followed meals and was preceded by severe non-radiating epigastric pain. During the past eight months he had become weak and had lost 40 pounds in weight.

His past history showed that he generally had good health. In 1918 he contracted a neisserian infection and syphilis. He received a course of 38 antisyphilitic injections (both intravenously and intramuscularly) at that time but had had none since. In 1933 he developed a urethral stricture with bladder stones and anuria. An external urethrotomy was performed and since that time he had had no urinary difficulties.

The family and marital histories were irrelevant. Physical examination showed moderate malnutrition. The Wassermann test was 4+; hemoglobin, 71 per cent, and white blood cell count, 4,850, with normal differential count.

Accessory clinical findings, revealed by repeated gastroscopic examination, included a large filling defect on the lesser curvature which was thought to be carcinoma. A gastro-intestinal series done on Feb. 24 revealed an irregular area 3 or 4 cm. in diameter just above the pylorus wherein the stomach wall was rigid. There was no retention (Fig. 1).

The original diagnosis was (1) carcinoma of the stomach and (2) syphilis, insufficiently treated.

The patient was given an intensive course of antisyphilitic therapy. Laparotomy was deferred, awaiting the outcome of the therapy. On March 10, 1938, the gastro-intestinal series was repeated. The lesion was a good deal smaller, but since there was considerable pylorospasm present it was not clear whether

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[2] Present address, Charlotte, N. C.

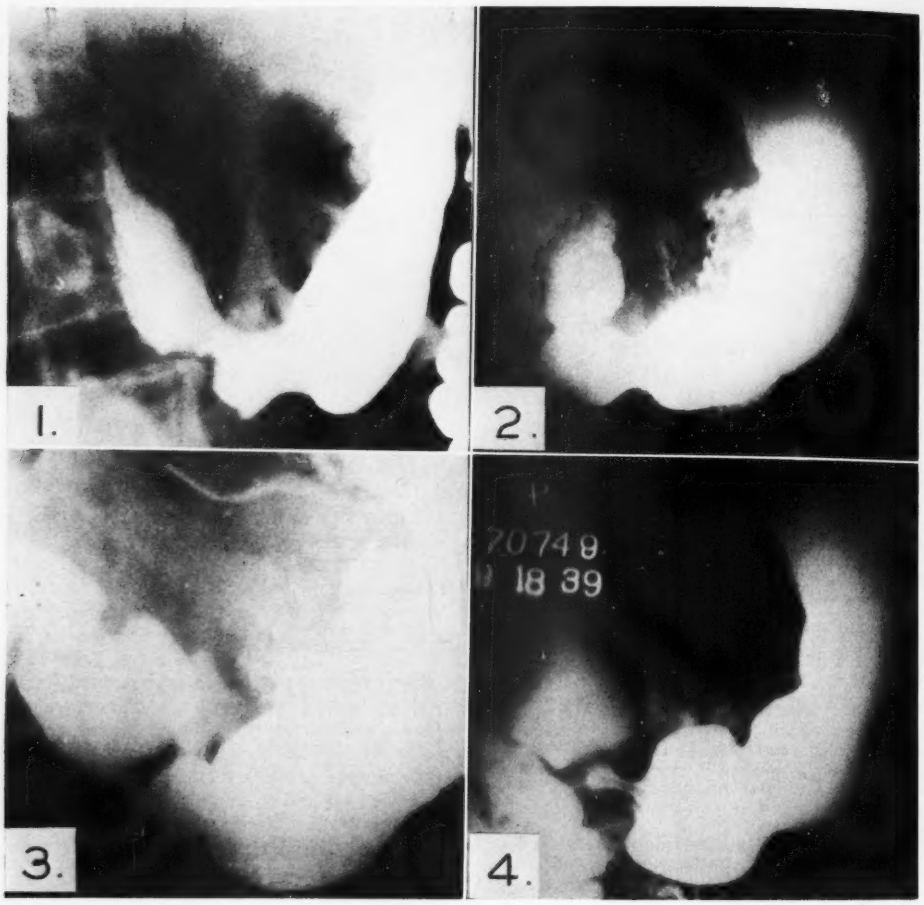

Fig. 1. The lesion as seen on our first examination. Note the irregularity of the prepyloric area.
Fig. 2. Disappearance of the lesion after three weeks of intensive antisyphilitic therapy. There was moderate pylorospasm.
Fig. 3. Essentially normal stomach after five months.
Fig. 4. Eighteen months' follow-up. The stomach is normal.

the pylorus was involved (Fig. 2). The patient was discharged on March 20 and told to return in three weeks for check-up.

He was next seen on May 2, 1938, at which time he was in good health, had gained weight, and had no gastric symptoms whatsoever. Re-examination of his stomach showed it to be normal (Fig. 3). Since that time the patient has continued to receive antisyphilitic therapy. He was last seen in September, 1939, at which time his stomach was normal (Fig. 4). The Wassermann test has remained positive.

Conclusion.—A case of gastric syphilis simulating carcinoma has been reported. The lesion was in the most common area (prepyloric) and responded rapidly to intensive antisyphilitic therapy even though the Wassermann remained positive.

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DOCTORS AND POLITICS

Time was, in the good old days, when the physician was looked up to by the citizens of his community as a sort of font of worldly wisdom. His advice and counsel were sought by his admiring neighbors in matters of health, domestic relations, and politics. As a fatherly imparter of practical wisdom, the old family doctor sometimes almost usurped the functions of the priest.

Admitting that the complexity of modern urban civilization has largely erased the intimate relationship which formerly existed between the doctor and his "families," it is nevertheless our premise that the physician can and should exert a more effective influence on political events than he does today. Before enlarging upon this premise, it is perhaps well that we define some terms.

The word "politics," we insist, should be shorn of that malodorous connotation which has attached to it as a result of the dubious practices of some of the more notorious big-city machines. Politics, or political science, is concerned with the conscious definite purpose of society to establish authority and to determine its functions. By "playing politics," our illustrious forefathers conceived our form of government; they established its authority and determined its functions. The doctor, like every other good citizen, has inherited a responsibility to exercise the rights and privileges by which the individuals of the state control its public policy. His educational advantages increase his responsibility in this regard and render his neglect of duty more reprehensible than less fortunate followers in the civic community.

It is in this enlightened meaning of the word that our political system is envied from abroad. It is this kind of responsible citizenship that prompted no less a cynic than G. B. Shaw to remark several years ago: "You in America should trust to that volcanic political instinct which I have divined in you."

Now, the chief political interest of doctors as citizens today concerns the so-called "socialization" of Medicine. Here is another term needing definition. It has been so bandied about since the days of Marx and Lasalle as to become completely bereft of meaning. The Socialist Party disowns the word. It means one thing in Petrograd and another in Peoria.

Socialism is a philosophy, and to "socialize" is to accomplish, in one way or another, that philosophy. The aim of the socialist is to replace competition by co-operation, and profit-seeking by "social service," whatever that may mean. A sober consideration of the socialist philosophy reveals two conspicuous facts: it requires a considerable degree of dictatorial authority in the state, and our own government has travelled a remarkable distance toward its realization.

Returning now to the interests of medical men; just what did our President mean when he said, on Oct. 31, 1940, "Neither the American people nor their government intend to socialize medical practice any more than they plan to socialize industry"? These were reassuring words to doctors. But, due to the unfortunate fact that the term "socialize" has an extremely fuzzy meaning, it is doubtful if anyone besides the President knows exactly what he meant by that statement.

Certainly he meant that the right to seek profit in the practice of their profession would not be denied doctors. But, did he mean that he was opposed to compulsory health insurance? Probably not.

In his message on the state of the Union, delivered to Congress on Jan. 6, the President declared that this was "no time to stop thinking about the social and economic problems," and, in itemizing the subjects which, in his opinion, the Congress should immediately take under consideration, he referred specifically to the "widening of opportunities for adequate medical care." Next day, Senator Robert F. Wagner, New York, announced that a comprehensive proposal for an expanded national health program in line with the President's recommendation was being prepared for introduction in Congress. Senator Wagner, it will be recalled, was author of the National Health Act, proposed to the 76th Congress for the implementation of the recommendations of the President's National Health Conference committee.

He also sponsored the National Hospital Construction Act. Neither of these bills reached a vote.

According to newspaper accounts, the Senator's new bill will combine both the previous ones. Included in the $90,000,000 appropriation for the first year, the bill will, according to reports, provide for $35,000,000 in contributions to states toward the operation of "approved plans for general medical care." It also would provide $9,000,000 for construction of federally owned hospitals. The U. S. Public Health Service and Federal Security Agency are reported to be working on a plan to offer federally financed health care to workers in defense industries.

Enactment of these legislative proposals may not amount to the "socialization" of Medicine. They would, nevertheless, provide for a considerable degree of political control over a large portion of medical practice in America. That is the very thing to which the medical profession has objected in opposing "socialized" Medicine or government-controlled health insurance. It is not compulsory health insurance per se that is objected to—it is the political control of medical practice which must perforce accompany a federally controlled system.

Whether or not "socialized" Medicine and compulsory health insurance are one and the same thing is a question we need not now debate. The point is that Medicine has always and will continue to object to any proposal that will place the delivery of medical care under the control of politicians. Doctors know that such a system would be contrary to the best interests of the public and that any advantages claimed for it would be more than offset by a host of palpable evils.

Which returns us to our original premise: that physicians should exert a more effective influence on political events than they do today. To protect the public welfare against politics in health, and to guard the profession of medicine against influences bound to retard its progress, doctors must take a more active interest in politics. No group outside the medical profession is competent to guide the policies of the government in matters of health. It is the responsibility of the medical profession to provide this guidance. Under our system of government there is one way, and only one way, that such responsibility can be exercised—and that is through political effort.

Two points must be understood if the political effort of individual doctors and medical organizations is going to have any effect upon the policies of the government. To appreciate them fully, it is going to be necessary that some firmly settled illusions be discarded. First, local politics is very much more important than national politics. Second, the primary is vastly more important than the general election. Any citizen can exert a great deal more influence upon the political trends of the national government by quietly interesting himself in the politics of his own neighborhood precinct than he can by writing brilliant letters to his congressman. Furthermore, he will find that the time to convince a politician regarding any fundamental issue is before the election, and not afterwards.

These are stirring times in America—times during which the cloak of "national defense" can be used to usher in radical innovations in the function of the national government. Now is the time for all good doctors to come to the aid of their nation. They can aid their country and protect the interests of the people by once more occupying a prominent place in the civic and political life of the community.

RADIOLOGICAL SOCIETIES IN NORTH AMERICA

Editor's Note.—Will secretaries of societies please cooperate with the Editor by supplying information for this section? Please send such information to Howard P. Doub, M.D., Henry Ford Hospital, Detroit, Mich.

UNITED STATES

CALIFORNIA

California Medical Association, Section on Radiology.—Chairman, Carl H. Parker, M.D., 65 N. Madison Ave., Pasadena; *Secretary,* Wilbur Bailey, M.D., 2007 Wilshire Blvd., Los Angeles.

Los Angeles County Medical Association, Radiological Section.—President, M. L. Pindell, M.D.; *Vice-president,* Richard T. Taylor, M.D.; *Secretary,* Wilbur Bailey, M.D., 2007 Wilshire Blvd.; *Treasurer,* Henry Snure, M.D., 1414 South Hope Street; Kenneth Davis, M.D., *Member of Executive Committee.* Meets second Wednesday of each month at County Society Building.

Pacific Roentgen Society.—Chairman, William E. Costolow, M.D., Los Angeles; *Members of Executive Committee,* I. S. Ingber, M.D., San Francisco; D. R. MacColl, M.D., Los Angeles, and J. D. Coate, M.D., Oakland; *Secretary-Treasurer,* L. Henry Garland, M.D., 450 Sutter St., San Francisco. Executive Committee meets quarterly; Society meets annually during annual meeting of the California Medical Association.

San Francisco Radiological Society.—Secretary, Harold A. Hill, M.D., 450 Sutter Street. Meets monthly on third Thursday at 7:45 P.M., for the first six months at Toland Hall (Univ. of Calif. Med. School) and for the second six months at Lane Hall (Stanford Univ. School of Med.).

COLORADO

Denver Radiological Club.—President, N. B. Newcomer, M.D., 306 Republic Bldg.; *Vice-president,* Elizabeth Newcomer, M.D.; *Secretary,* Paul R. Weeks, M.D., 520 Republic Bldg.; *Treasurer,* L. G. Crosby, M.D., 366 Metropolitan Bldg. Meets third Friday of each month at homes of members.

CONNECTICUT

Connecticut State Medical Society, Section on Radiology.—Chairman, Owen J. Groark, M.D., 881 Lafayette St., Bridgeport; *Secretary-Treasurer,* Max Climan, M.D., 242 Trumbull St., Hartford. Meetings bimonthly, on second Thursday. Place of meeting selected by Secretary.

DELAWARE

Affiliated with Philadelphia Roentgen Ray Society.

FLORIDA

Florida Radiological Society.—President, J. H. Lucinian, M.D.; *Vice-president,* John N. Moore, M.D.; *Secretary-Treasurer,* Elliott M. Hendricks, M.D., 314 Sweet Bldg., Fort Lauderdale. The next meeting will be at the time of the annual meeting of the Medical Association of Florida in the spring.

GEORGIA

Georgia Radiological Society.—President, Robert Drane, M.D., DeRenne Apts., Savannah; *Vice-president,* J. J. Collins, M.D., Archbold Hospital, Thomasville; *Secretary-Treasurer,* Robert C. Pendergrass, M.D., Prather Clinic Bldg., Americus. Meetings twice annually, in November and at the annual meeting of the Medical Association of Georgia in the spring.

ILLINOIS

Chicago Roentgen Society.—President, Adolph Hartung, M.D.; *Vice-president,* Warren W. Furey, M.D.; *Secretary,* Chester J. Challenger, M.D., 3117 Logan Blvd. The Society meets at the Palmer House on the second Thursday of October, November, January, February, March, and April.

Illinois Radiological Society.—President, Harry W. Ackeman, M.D., 321 W. State St., Rockford; *Vice-president,* D. R. Hanley, M.D., St. Mary's Hospital, Streator; *Secretary-Treasurer,* William DeHollander, M.D., St. John's Hospital, Springfield. Meetings quarterly by announcement.

Illinois State Medical Society, Section on Radiology.—Chairman, Harry W. Ackeman, M.D., 321 W. State St., Rockford; *Secretary,* Earl E. Barth, M.D., 303 E. Chicago Ave., Chicago.

INDIANA

The Indiana Roentgen Society.—President, H. H. Inlow, M.D., Shelbyville; *President-elect,* Charles Wyeth, M.D., Terre Haute; *Vice-president,* C. A. Stayton, M.D., Indianapolis; *Secretary-Treasurer,* Clifford C. Taylor, M.D., 23 E. Ohio St., Indianapolis. Annual meeting in May.

IOWA

The Iowa X-ray Club.—Holds luncheon and business meeting during annual session of Iowa State Medical Society.

KENTUCKY

Kentucky Radiological Society.—President, D. B. Harding, M.D., Lexington; *Vice-president,* I. T. Fugate, M.D., Louisville; *Secretary-Treasurer,* Joseph C. Bell, M.D., 402 Heyburn Bldg., Louisville. Meeting annually in Louisville, third Sunday afternoon in April

LOUISIANA

Shreveport Radiological Club.—President, C. P. Rutledge, M.D.; *Vice-president,* S. C. Barrow, M.D.; *Secretary-Treasurer,* W. R. Harwell, M.D. Meetings monthly on the second Wednesday, at the offices of the various members.

MAINE

See New England Roentgen Ray Society.

MARYLAND

Baltimore City Medical Society, Radiological Section.—Chairman, John W. Pierson, M.D., 1107 St. Paul St.; *Secretary*, Walter L. Kilby, M.D., 101 W. Read St. Meetings are held the third Tuesday of each month.

The Thirty-first Annual Midwinter Conference of Eastern Radiologists will meet in Baltimore on Jan. 31 and Feb. 1, 1941.

MASSACHUSETTS

See New England Roentgen Ray Society.

MICHIGAN

Detroit X-ray and Radium Society.—President, O. J. Shore, M.D., 552 Fisher Bldg., Detroit; *Vice-president*, Clarence E. Hufford, M.D., 421 Michigan St., Toledo, Ohio; *Secretary-Treasurer*, E. R. Witwer, M.D., Harper Hospital, Detroit. Meetings first Thursday of each month from October to May, inclusive, at Wayne County Medical Society club rooms, 4421 Woodward Ave., Detroit.

Michigan Association of Roentgenologists.—President, J. H. Dempster, M.D., Detroit; *Vice-president*, L. E. Holly, M.D., Muskegon; *Secretary-Treasurer*, J. E. Lofstrom, M.D., 1536 David Whitney Bldg., Detroit. Meetings quarterly by announcement.

MINNESOTA

Minnesota Radiological Society.—President, Harry Weber, M.D., Mayo Clinic, Rochester; *Vice-president*, G. T. Nordin, M.D., Minneapolis; *Secretary*, John P. Medelman, M.D., 572 Lowry Medical Arts Bldg., St. Paul. Meetings quarterly.

MISSOURI

The Kansas City Radiological Society.—President, Galen M. Tice, M.D., Univ. of Kansas Hospitals, Kansas City, Kansas; *Secretary*, P. E. Hiebert, M.D., 907 North Seventh St. (Huron Bldg.), Kansas City, Kansas. Meetings last Thursday of each month.

The St. Louis Society of Radiologists.—President, Oscar C. Zink, M.D., St. Luke's Hospital; *Secretary*, Wilbur K. Mueller, M.D., University Club Bldg. Meets on fourth Wednesday of October, January, March, and May, at a place designated by the president.

NEBRASKA

Nebraska Radiological Society.—President, H. A. Scott, M.D., Veterans Administration Facility, Lincoln; *Secretary*, D. A. Dowell, M.D., 816 Medical Arts Bldg., Omaha. Meetings third Wednesday of each month at 6 P.M. in either Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY

(Maine, New Hampshire, Vermont, Massachusetts, and Rhode Island.) *Secretary*, Hugh F. Hare, M.D., Lahey Clinic, Boston, Mass. Meets monthly on third Friday at Boston Medical Library.

NEW HAMPSHIRE

See New England Roentgen Ray Society.

NEW JERSEY

Radiological Society of New Jersey.—President, James G. Boyes, M.D., 912 Prospect Ave., Plainfield; *Vice-president*, Nathan J. Furst, M.D., 190 Johnson Ave., Newark; *Secretary*, W. James Marquis, M.D., 198 Clinton Ave., Newark; *Treasurer*, H. A. Vogel, M.D., 1060 East Jersey St., Elizabeth, and *Counsellor*, H. J. Perlberg, M.D., 921 Bergen Ave., Jersey City. Meetings at Atlantic City at time of State Medical Society and Midwinter in Newark as called by president.

NEW YORK

Associated Radiologists of New York, Inc.—President, I. J. Landsman, M.D., 910 Grand Concourse, New York City; *President-elect*, D. E. Ehrlich, M.D., 35 West 92nd St., New York City; *Vice-president*, Frederic E. Elliott, M.D., 122 76th St., Brooklyn; *Treasurer*, Solomon Fineman, M.D., 133 East 58th St., New York City; *Secretary*, William J. Francis, M.D., 210 Fifth Ave., New York City. Regular meetings the first Monday evening of the month in March, May, October, and December.

Brooklyn Roentgen Ray Society.—President, A. L. L. Bell, M.D., Long Island College Hospital, Henry, Pacific, and Amity Sts.; *Secretary-Treasurer*, L. J. Taormina, M.D., 1093 Gates Ave. Meetings held the fourth Tuesday of every month, October to April.

Buffalo Radiological Society.—President, Edward Koenig, M.D., 100 High St., Buffalo; *Vice-president*, W. Roger Scott, M.D., 598 Pine St., Niagara Falls; *Secretary-Treasurer*, Joseph S. Gian-Franceschi, M.D., 610 Niagara St. Meetings second Monday evening each month, October to May, inclusive.

Central New York Roentgen Ray Society.—President, Albert Lenz, M.D., 613 State St., Schenectady; *Vice-president*, Dwight V. Needham, M.D., 123 Sedgwick St., Syracuse; *Secretary-Treasurer*, Carlton F. Potter, M.D., 425 Waverly Ave., Syracuse. Meetings are held in January, May, and October, as called by Executive Committee.

Long Island Radiological Society.—President, Samuel G. Schenck, M.D., Brooklyn; *Vice-president*, G. Henry Koiransky, M.D., Long Island City; *Secretary*, Marcus Wiener, M.D., 1430 48th St., Brooklyn; *Treasurer*, Louis Goldfarb, M.D., 608 Ocean Ave., Brooklyn. Meetings fourth Thursday evening each month at Kings County Medical Bldg.

New York Roentgen Society.—President, Henry K. Taylor, M.D., 667 Madison Ave., New York City;

Vice-president, Roy D. Duckworth, M.D., 170 Maple Ave., White Plains, N. Y.; *Secretary*, Eric J. Ryan, M.D., St. Luke's Hospital, New York City, and *Treasurer*, Paul C. Swenson, M.D., 168th St. and Broadway, New York City.

Rochester Roentgen-ray Society.—Chairman, George H. S. Ramsey, M.D., 277 Alexander St.; *Secretary*, S. C. Davidson, M.D., 277 Alexander St. Meetings at convenience of committee.

NORTH CAROLINA

Radiological Society of North Carolina.—President, Robert P. Noble, M.D., 127 W. Hargett St., Raleigh; *Vice-president*, A. L. Daughtridge, M.D., 144 Coast Line St., Rocky Mount; *Secretary-Treasurer*, Major I. Fleming, M.D., 404 Falls Road, Rocky Mount. Meetings with State meeting in May, and meeting in October.

OHIO

Ohio Radiological Society.—President, U. V. Portmann, M.D., Cleveland; *Secretary*, J. E. McCarthy, M.D., Cincinnati. A committee was appointed to draw up a constitution and by-laws. The next meeting will be held at the time and place of the annual meeting of the Ohio State Medical Association.

Cleveland Radiological Society.—President, L. A. Pomeroy, M.D., Hanna Bldg., Cleveland; *Vice-president*, P. C. Langan, M.D., 215 Wellesley Ave., Akron; *Secretary-Treasurer*, H. A. Mahrer, M.D., 10515 Carnegie Ave., Cleveland. Meetings at 6:30 P.M. at the Mid-day Club, in the Union Commerce Bldg., on fourth Monday of each month from October to April, inclusive.

Radiological Society of the Academy of Medicine (Cincinnati Roentgenologists).—*President*, Samuel Brown, M.D.; *Secretary-Treasurer*, Justin E. McCarthy, M.D., 707 Race St. Meetings held third Tuesday of each month.

PENNSYLVANIA

Pennsylvania Radiological Society.—President, H. Norton Mawhinney, M.D., Pittsburgh; *President-elect*, Peter B. Mulligan, M.D., Ashland; *First Vice-president*, Harold S. Callen, M.D., Bradford; *Second Vice-president*, Harold W. Jacox, M.D., Pittsburgh; *Secretary-Treasurer*, L. E. Wurster, M.D., 416 Pine St., Williamsport; *Editor*, William E. Reiley, M.D., Clearfield; *Assistant Editor*, Sydney J. Hawley, M.D., Danville; *Censor for Three Years*, A. R. Snedden, M.D., McKeesport. The Society meets annually; time and place of next meeting will be announced later.

The Philadelphia Roentgen Ray Society.—President, Jacob H. Vastine, II, M.D., Medical Arts Bldg., Philadelphia; *Vice-president*, A. Maxwell Sharpe, M.D., 708 Sproul St., Chester; *Secretary*, Barton R. Young, M.D., Temple University Hospital, Philadelphia; *Treasurer*, Fay K. Alexander, M.D., Chestnut Hill Hospital, Philadelphia. Meetings held first Thursday of each month at 8:15 P.M., from October to May, in Thomson Hall, College of Physicians, 21 S. 22nd St., Philadelphia.

The Pittsburgh Roentgen Society.—President, Paul G. Bovard, M.D., 306 Corbett St., Tarentum, Pa.; *Vice-president*, John H. Gemmell, M.D., 262 Connecticut Ave., Rochester, Pa., and *Secretary-Treasurer*, Harold W. Jacox, M.D., 4800 Friendship Ave., Pittsburgh, Pa. Meetings are held on the second Wednesday of each month at 4:30 P.M., from October to June, at the Pittsburgh Academy of Medicine, 322 N. Craig St.

RHODE ISLAND

See New England Roentgen Ray Society.

SOUTH CAROLINA

South Carolina X-ray Society.—President, T. A. Pitts, M.D., Columbia; *Secretary-Treasurer*, Malcolm Mosteller, M.D., Columbia Hospital, Columbia. Meetings in Charleston on first Thursday in November, also at time and place of South Carolina State Medical Association.

SOUTH DAKOTA

Meets with Minnesota Radiological Society.

TENNESSEE

Memphis Roentgen Club.—Chairmanship rotates monthly in alphabetical order. Meetings second Tuesday of each month at University Center.

Tennessee Radiological Society.—President, Eugene Abercrombie, M.D., 305 Medical Arts Bldg., Knoxville; *Vice-president*, Christopher C. McClure, M.D., 404 Doctors Bldg., Nashville; *Secretary-Treasurer*, Franklin B. Bogart, M.D., 311 Medical Arts Bldg., Chattanooga. Meeting annually with State Medical Society in April.

TEXAS

Texas Radiological Society.—President, C. F. Crain, M.D., Corpus Christi; *President-elect*, M. H. Glover, M.D., Wichita Falls; *First Vice-president*, G. D. Carlson, M.D., Dallas; *Second Vice-president*, P. E. Wigby, M.D., Dallas; *Secretary-Treasurer*, L. W. Baird, M.D., Scott and White Hospital, Temple. Meets annually. The next annual meeting is to be Jan. 18, 1941, in Sherman.

VERMONT

See New England Roentgen Ray Society.

VIRGINIA

Virginia Radiological Society.—President, Wright Clarkson, M.D., Petersburg· *Vice-president*, Clayton

W. Ely, M.D., Norfolk; *Secretary*, Charles H. Peterson, M.D., 603 Medical Arts Bldg., Roanoke.

WASHINGTON

Washington State Radiological Society.—President, H. E. Nichols, M.D., Stimson Bldg., Seattle; *Vice-president*, George Cornett, M.D., Yakima; *Secretary-Treasurer*, Kenneth J. Holtz, M.D., American Bank Bldg., Seattle. Meetings fourth Monday of each month at College Club, Seattle.

WISCONSIN

Milwaukee Roentgen Ray Society.—President, H. W. Hefke, M.D.; *Vice-president*, Frederick C. Christensen, M.D.; *Secretary-Treasurer*, Irving I. Cowan, M.D., Mount Sinai Hospital, Milwaukee. Meets monthly on first Friday at the University Club.

Radiological Section of the Wisconsin State Medical Society.—Secretary, Russel F. Wilson, M.D., Beloit Municipal Hospital, Beloit. Two-day annual meeting in May and one day in connection with annual meeting of State Medical Society, in September.

University of Wisconsin Radiological Conference.—Secretary, E. A. Pohle, M.D., 1300 University Ave., Madison, Wis. Meets every Thursday from 4 to 5 P.M., Room 301, Service Memorial Institute.

CANADA

Section on Radiology, Canadian Medical Association.—Chairman, Gordon Richards, M.D., Medical Arts Bldg., Toronto; *Secretary*, W. J. Cryderman M.D., Medical Arts Bldg., Toronto.

Section on Radiology, Ontario Medical Association.—Chairman, E. H. Shannon, M.D., St. Michael's Hospital, Toronto; *Secretary*, W. J. Cryderman, M.D., 474 Glenlake Avenue, Toronto.

Canadian Association of Radiologists.—President, J. E. Gendreau, M.D., Montreal; *Vice-president*, W. H. McGuffin, M.D., Calgary; *Honorary Secretary-Treasurer*, A. C. Singleton, M.D., Toronto; *Chairman of Interrelations Committee*, W. A. Jones, M.D., Kingston.

La Société Canadienne-Française d'Electrologie et de Radiologie Médicales held a meeting at Quebec on Sept. 28, 1940, at which time the following officers were elected for the next two years: *President*, Albert Comtois, M.D., Hôpital Ste.-Justine, Montreal; *First Vice-president*, Jules Gosselin, M.D., Hôpital St.-Sacrement, Quebec; *Second Vice-president*, Paul Brodeur, M.D., General Hospital, Ottawa; *General Secretary*, Origène Dufresne, M.D., Institut du Radium, Montreal, and *General Treasurer*, Doriva Léonard, M.D., Hôpital Notre Dame, Montreal. Meetings are held the third Saturday of each month, generally at the Radium Institute, 4120 East Ontario Street, Montreal; sometimes, at homes of members.

CUBA

Sociedad de Radiología y Fisioterapía de Cuba.—Offices in Hospital Mercedes, Havana. Meetings are held monthly.

EDITORIAL

HOWARD P. DOUB, M.D., *Editor* JOHN D. CAMP, M.D., *Associate Editor*

DR. MENVILLE RETIRES AS EDITOR

It is with regret that the officers and Publication Committee of the Radiological Society of North America announce the resignation of Dr. Leon J. Menville as Editor of RADIOLOGY, a position that he has held since June, 1931. Dr. Menville has been deeply interested in the affairs of the Society and Journal for many years and, in recognition of his service to the Society and to the science of Radiology, was unanimously chosen as President-elect at the recent annual meeting in Cleveland.

Dr. Menville assumed the editorship of RADIOLOGY in what might be called the inflationary period of the Journal. He not only guided it safely through a rather trying stage of deflation but brought about constant improvements which have enabled RADIOLOGY to keep pace with the changing standards of medical literature. These accomplishments are imperishably reflected in the volumes of the Journal for the past ten years and are well known to all.

In his professional life, Dr. Menville has always been a firm advocate of the importance and value of organized medicine and has devoted much of his time and energy to it. He is a Past President of the Louisiana State Medical Society. For many years he served as President of the Louisiana State Board of Medical Examiners and the period of his administration was marked by much constructive work and by an exemplary Medical Practice Act. He is a Fellow of the American Medical Association and at present is a delegate to that body, representing the Louisiana State Medical Society. He is also an honored member of many other clinical and radiological societies.

Dr. Menville served as a representative of the Radiological Society of North America on the first examining board of the American Board of Radiology. In addition he has been a member of the Editorial Board of the *American Journal of Cancer* for a number of years.

Throughout his medical career, Dr. Menville has shown a great interest in medical education. Since 1918 he has been a member of the faculty of Tulane Medical School as instructor, assistant professor, and professor of radiology (1934). During the past year his ability as a radiologist, teacher and leader in his state has been recognized and signalized by his appointment as Director of the Department of Radiology of Charity Hospital in New Orleans. This well equipped hospital of 3,700 beds is one of the largest outstanding institutions in the country. We know that Dr. Menville will give to his new work the same devotion and enthusiasm that marked his office as Editor of RADIOLOGY, and to him, as he assumes his new duties, we extend our congratulations and best wishes.

In assuming the position of Editor we shall endeavor to carry on the work in a manner which will reflect credit on the Radiological Society and on Radiology in general. We are conscious of the high degree of excellence which RADIOLOGY has attained under the able editorship of Dr. Menville and shall make every effort to maintain this standard.

To Dr. Menville we wish to extend our sincere appreciation of the many kindnesses which he has shown us during the years of our association on the editorial staff, and especially of his invaluable help during the transition period incident to moving the editorial office. We bespeak the benefit of his wise counsel in our future work.

THE AMERICAN BOARD OF RADIOLOGY

The next examination given by The American Board of Radiology will be held at the Hotel Statler in Cleveland, Ohio, May 30, May 31, and June 1, 1941. Those who intend to be examined in Cleveland should have their applications on file with the Secretary at least two months before the examination. It is also suggested that, in view of the fact that the Hotel Statler will be the radiologic headquarters, those who wish reservations should write directly to Mr. Richard D. McLain, Hotel Statler, at their earliest convenience.

B. R. KIRKLIN, *Secretary*
The Mayo Clinic
Rochester, Minnesota

The following is a list of those who have been certified or granted additional certification during 1940:

1. Abraham, Adolph, New York, N. Y., *Radiology*
2. Addington, Ercell A., Spokane, Wash., *Radiology*
3. Africano, Scipio H., Union City, N. J., *Diagnostic Roentgenology*
4. Andersen, L. Milford, Brooklyn, N. Y., *Roentgenology*
5. Armao, Joseph, Philadelphia, Pa., *Radiology*
6. Armbruster, John L., Milwaukee, Wisc., *Radiology*
7. Aulls, Ernest C., Washington, D. C., *Roentgenology*
8. Avery, Roscoe E., Barre, Vt., *Diagnostic Roentgenology*
9. Barrett, Henry A., New York, N. Y., *Radiology*
10. Beckstrand, Grant H., Long Beach, Calif., *Therapeutic Radiology*
11. Berman, Theodore M., Miami Beach, Fla., *Diagnostic Roentgenology*
12. Bettelheim, Frederick, New York, N. Y., *Radiology*
13. Bird-Acosta, Ignacio, Ithaca, N. Y., *Roentgenology*
14. Borow, Louis, Bound Brook, N. J., *Radiology*
15. Bowing, Irwin E., Kenosha, Wisc., *Roentgenology*
16. Boyer, Helene N., Racine, Wisconsin, *Radiology*
17. Brannon, Donald D., Cleveland, Ohio, *Roentgenology*
18. Brown, James M., San Francisco, Calif., *Radiology*
19. Brown, Webster H., Baltimore, Md., *Radiology*
20. Bull, Robert G., White Plains, N. Y., *Roentgenology*
21. Burton, William Y., Portland, Ore., *Radiology*
22. Camiel, Mortimer R., Brooklyn, N. Y., *Therapeutic Radiology*
23. Cashion, William R., Jamaica, L. I., N. Y., *Radiology*
24. Christy, Christ J., Buffalo, N. Y., *Therapeutic Radiology*
25. Connolly, Joseph P., Stamford, Conn., *Radiology*
26. Cooper, Jesse R., Newcastle, Pa., *Radiology*
27. Crawford, J. Ramser, Flushing, L. I., N. Y., *Diagnostic Roentgenology*
28. Danelius, Gerhard, Chicago, Ill., *Roentgenology*
29. Davenport, Carroll S., Lansing, Mich., *Radiology*
30. deLalla, Emanuel, Utica, N. Y., *Roentgenology*
31. Delano, Percy Joseph, Chicago, Ill., *Radiology*
32. Dirks, Maitland S., Iowa City, Ia., *Radiology*
33. Dodds, Wemple, Crawfordsville, Ind., *Radiology*
34. Eberhard, Theodore P., Columbia, Mo., *Therapeutic Radiology*
35. Edson, George N., Jackson Heights, L. I., N. Y., *Diagnostic Roentgenology*
36. Ehrenpreis, Bernard, Brooklyn, N. Y., *Radiology*
37. Elsey, Edward C., Cincinnati, Ohio, *Radiology*
38. Emery, Clyde K., Los Angeles, Calif., *Therapeutic Radiology*
39. Farrow, Joseph H., New York, N. Y., *Therapeutic Radiology*
40. Feaster, Annette M. B., St. Petersburg, Fla., *Therapeutic Radiology*
41. Felson, Benjamin, Indianapolis, Ind., *Radiology*
42. Ferrucci, Joseph, Framingham, Mass., *Diagnostic Roentgenology*
43. Fuchlow, J. Richard, Rapid City, S. D., *Roentgenology*
44. Galligan, Charles A., Jr., Monterey, Calif., *Diagnostic Roentgenology*
45. Galluccio, Anthony C., Bronx, N. Y., *Diagnostic Roentgenology*
46. Garcia, Manuel, New Orleans, La., *Therapeutic Radiology*
47. Gemmill, James R., Monessen, Pa., *Diagnostic Roentgenology*
48. Gibbon, William H., Sioux City, Ia., *Radiology*
49. Gilmer, William P., Clifton Forge, Va., *Roentgenology*
50. Glaser, Leland F., Springfield, Mo., *Radiology*
51. Goldberg, Benjamin, Chicago, Ill., *Diagnostic Roentgenology*
52. Goldblum, Jacob, Uniontown, Pa., *Radiology*
53. Golding, Harry N., Paterson, N. J., *Diagnostic Roentgenology*
54. Governale, Vincent J., Long Beach, N. Y., *Diagnostic Roentgenology*
55. Graves, A. Judson, Jacksonville, Fla., *Radiology*
56. Gray, Edwin F., Terre Haute, Ind., *Radiology*
57. Greene, Theodore C., Tsinan Shantung, China, *Diagnostic Roentgenology*
58. Grossman, Abraham, Chicago, Ill., *Therapeutic Radiology*
59. Guillium, William H., Asbury Park, N. J., *Roentgenology*
60. Hames, Frederick W., Pine Bluff, Ark., *Therapeutic Radiology*
61. Hamilton, Charles C., Claremont, N. H., *Roentgenology*
62. Harrington, Leo A., Brooklyn, N. Y., *Radiology*
63. Hartzell, Homer V., Jr., Seattle, Wash., *Radiology*
64. Hayden, Edward M., Tucson, Ariz., *Diagnostic Roentgenology*
65. Hayes, Arthur W., Greenfield, Mass., *Roentgenology*
66. Held, Louis A., Brooklyn, N. Y., *Diagnostic Roentgenology*
67. Helper, Norton, Ann Arbor, Mich., *Radiology*
68. Herendeen, Ralph E., New York, N. Y., *Radiology*
69. Hinkel, Charles L., New York, N. Y., *Radiology*
70. Holding, Arthur F., Albany, N. Y., *Radiology*
71. Hrdlicka, George R., Brooklyn, N. Y., *Roentgenology*
72. Hulst, Henry, Grand Rapids, Mich., *Radiology*
73. Huston, Harold C., Eau Claire, Wisc., *Radiology*
74. Huyler, Washington C., New York, N. Y., *Diagnostic Roentgenology*
75. Jaffe, Henry L., Chicago, Ill., *Therapeutic Radiology*

76. Jamison, Horace W., Los Angeles, Calif., *Radiology*
77. Jares, John James, Jr., Sarasota, Fla., *Radiology*
78. Johns, Miles W., Utica, N. Y., *Diagnostic Roentgenology*
79. Johnson, Samuel H., Miami, Fla., *Roentgenology*
80. Johnston, Albert C., Berlin, N. H., *Roentgenology*
81. Johnston, George C., Orlando, Fla., *Radiology*
82. Kahlstrom, Samuel C., Bath, N. Y., *Diagnostic Roentgenology*
83. Keddy, Russell A., Stamford, Conn., *Radiology*
84. Kegerreis, Roy, Elmhurst, Ill., *Radiology*
85. Kimble, J. Norman, Takoma Park, Maryland, *Diagnostic Roentgenology*
86. Kok, Harry, Benton Harbor, Mich., *Radiology*
87. Krause, George R., Cleveland, Ohio, *Roentgenology*
88. Kresch, Philip, Bayonne, N. J., *Diagnostic Roentgenology*
89. Landsman, Isadore J., New York, N. Y., *Diagnostic Roentgenology*
90. Lawrason, Douglas M., Albuquerque, N. M., *Radiology*
91. Ledbetter, Llewellyn H., Beaumont, Tex., *Diagnostic Roentgenology*
92. LeMone, David V., Columbia, Mo., *Diagnostic Roentgenology*
93. Levin, Ralph T., New York, N. Y., *Radiology*
94. Lieff, Abraham, New York, N. Y., *Therapeutic Radiology*
95. Liljencrantz, Eric, San Francisco, Calif., *Therapeutic Radiology*
96. Lowman, Robert M., Philadelphia, Pa., *Radiology*
97. Marting, Esther C., Cincinnati, Ohio, *Therapeutic Radiology*
98. Meachen, John W., Boston, Mass., *Roentgenology*
99. Mendelson, Emanuel, Brooklyn, N. Y., *Radiology*
100. Merrill, Walter H., Glenn Dale, Md., *Radiology*
101. Merrit, William H., New York, N. Y., *Radiology*
102. Meyers, Paul T., New York, N. Y., *Radiology*
103. Miller, Albert, Rochester, Minn., *Radiology*
104. Miller, Earl R., New Haven, Conn., *Radiology*
105. Miller, John Francis, Johnson City, N. Y., *Radiology*
106. Miller, Lawson E., New York, N. Y., *Roentgenology*
107. Miller, Wallace C., Boston, Mass., *Radiology*
108. Minton, Russell F., Ardmore, Pa., *Diagnostic Roentgenology*
109. Morrison, Harvey R., Boston, Mass., *Radiology*
110. Mucci, Lawrence A., New Britain, Conn., *Radiology*
111. Mufson, Samuel, New York, N. Y., *Diagnostic Roentgenology*
112. Nessa, Curtis B., Minneapolis, Minn., *Radiology*
113. O'Hara, Fred Summa, Springfield, Ill., *Radiology*
114. Olds, John W., San Diego, Calif., *Radiology*
115. Perillo, Januarius A., Olean, N. Y., *Roentgenology*
116. Petersen, Arthur S. J., Chicago, Ill., *Roentgenology*
117. Pinkston, Beth Tollan, Los Angeles, Calif., *Radiology*
118. Pinner, William E., Philadelphia, Pa., *Radiology*
119. Popoff, George D., Buffalo, N. Y., *Roentgenology*
120. Potozky, Henry, New York, N. Y., *Therapeutic Radiology*
121. Root, Joseph C., Cleveland, Ohio, *Roentgenology*
122. Rosenblate, Adolph J., Chicago, Ill., *Roentgenology*
123. Rossitto, Anthony F., Wichita, Kan., *Radiology*
124. Roswit, Bernard, New York, N. Y., *Therapeutic Radiology*
125. Sagel, Jacob, Gary, Ind., *Roentgenology*
126. Schlein, William, Brooklyn, N. Y., *Roentgenology*
127. Schulz, Milford D., Boston, Mass., *Roentgenology*
128. Scott, Lawrence D., Nashville, Tenn., *Radiology*
129. Seedorf, Everett E., LaCrosse, Wisc., *Radiology*
130. Shapiro, Abraham V., New York, N. Y., *Radiology*
131. Sharp, George S., Pasadena, Calif., *Therapeutic Radiology*
132. Sheedy, Leo P., Pittsburgh, Pa., *Radiology*
133. Sinberg, Samuel E., New York, N. Y., *Roentgenology*
134. Smith, Jesse W., Bishop, Honolulu, Hawaii, *Radiology*
135. Springer, Floyd A., Des Moines, Ia., *Therapeutic Radiology*
136. Squire, Everett W., Charleston, W. Va., *Radiology*
137. Staderman, Albert H., Philadelphia, Pa., *Roentgenology*
138. Stein, George H., Elizabeth, N. J., *Diagnostic Roentgenology*
139. Stein, Joseph, Hawthorne, N. Y., *Radiology*
140. Stewart, Calvin L., Abington, Pa., *Radiology*
141. Strusinski, Nicholas D., Jackson Heights, L. I., N. Y., *Diagnostic Roentgenology*
142. Sullivan, Joseph V., Flushing, L. I., N. Y., *Radiology*
143. Thorner, Rosalind, Philadelphia, Pa., *Radiology*
144. Truog, Clarence P., Miami, Fla., *Radiology*
145. Tschetter, David J., Canton, Ohio, *Radiology*
146. Tulisalo, Oscar W., Atlanta, Ga., *Radiology*
147. Vance, Lewis A., Boston, Mass., *Diagnostic Roentgenology*
148. Vanlandingham, Homer W., Rockford, Ill., *Radiology*
149. Wang, Shao-hsun, Peiping, China, *Radiology*
150. Ward, Leo J., Elizabeth, N. J., *Radiology*
151. Waskow, William L., Chicago, Ill., *Roentgenology*
152. West, Warren B., Champaign, Ill., *Radiology*
153. Wickham, Jacob M., Iowa City, Ia., *Radiology*
154. Williams, James N., Fort Leavenworth, Kans., *Radiology*
155. Willis, Augusta E., Orangeburg, S. C., *Radiology*
156. Wissing, Egon G., Boston, Mass., *Roentgenology*
157. Wood, John P., Pearl Harbor, Hawaii, *Roentgenology*
158. Woutat, Philip H., Grand Forks, N. D., *Radiology*
159. Zaretzki, Louis E., Brooklyn, N. Y., *Radiology*
160. Zwerling, Henry B., Philadelphia, Pa., *Radiology*

ANNOUNCEMENTS

EDITORIAL CHANGES

The Publication Committee announces the retirement of Miss Mary Inglehart as assistant to the editor of RADIOLOGY. Miss Inglehart has been associated with the Journal since its first issue in 1923 and, as assistant to Dr. Maximilian J. Hubeny and later Dr. Leon J. Menville, has shown unswerving devotion to the affairs of the editorial office and Journal. The volumes of RADIOLOGY published during her association with it bear the imprint of her editorial skill and permanently reflect her diligence and care in the discharge of her duties. We regret that ill health has necessitated her retirement from the activities of the editorial office.

The Editor and Publication Committee announce the appointment of Miss Marion B. Crowell as editorial assistant to succeed Miss Mary Inglehart, who has retired. Miss Crowell comes to RADIOLOGY after a long experience in the medical editorial field, having more recently been in charge of the editorial office of the *American Journal of Cancer*, which has currently ceased publication. With this experience in a field of medical literature that is intimately related to radiology, Miss Crowell is, we believe, particularly fitted to carry on the work of our editorial office.

IN MEMORIAM

JOSEPH WARRINGTON CRAWFORD, M.D.

1872–1940

Another of the pioneer roentgenologists of this country has passed from our midst. Dr. Joseph W. Crawford of North Adams, Mass., died in November, 1940, at his home in North Adams.

Dr. Crawford was born in Philadelphia on Oct. 17, 1872. He was educated in the local schools and later graduated from the Hahnemann Medical College in 1900. Shortly after that time he began practice in North Adams and became a member of the North Adams Hospital Staff. During his early medical work he interested himself in roentgenology and acquired the first x-ray machine in his community. Since that time he has been Roentgenologist of the North Adams Hospital as well as a member of the cancer clinic of that institution.

Dr. Crawford was a member of the Northern Berkshire Medical Society, the Massachusetts Medical Society, the American Medical Association, and the Radiological Society of North America.

CHARLES THURSTON HOLLAND

Word has been received of the death of Dr. Charles Thurston Holland in Liverpool, on January 16th. Dr. Holland was one of the pioneers in Roentgenology and his contributions to roentgenological literature span a period of forty years. He was Lecturer on Radiology at Liverpool University until his retirement in 1931, and was President of the First International Congress of Radiology, held in London in 1925. He was a Fellow of the American College of Radiology, and an Honorary Member of the American Roentgen Ray Society.

During the World War, Dr. Holland was a member of the War Office Committee on Radiology. He was also radiologist to the First Western General Hospital from 1914 to 1918, and for many years radiologist to the Royal Infirmary in Liverpool. In 1929–1930 he was President of the British Institute of Radiology.

His passing creates a feeling of deep personal loss to his many friends in America.

BOOKS RECEIVED

Books received are acknowledged under this heading, and such notice may be regarded as an acknowledgment of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

RADIOLOGIC PHYSICS. By CHARLES WEYL, S. REID WARREN, JR., AND DALLETT B. O'NEILL, Moore School X-ray Laboratory, Moore School of Electrical Engineering, University of Pennsylvania. With a Foreword by EUGENE P. PENDERGRASS, M.D., Director of the Department of Radiology, University of Pennsylvania. A volume of 459 pages with 158 figures. Published by Charles C. Thomas, Springfield, Illinois, 1941. Price: $5.50.

RADIOLOGY PHYSICS. An Introductory Course for Medical or Premedical Students and for All Radiologists. By JOHN KELLOCK ROBERTSON, F.R.S.C.,

Professor of Physics, Queen's University, Kingston, Canada. A volume of 270 pages with 188 figures. Published by D. Van Nostrand Company, Inc., New York, N. Y., 1941. Price: $3.50.

AGE MORPHOLOGY OF PRIMARY TUBERCLES. By HENRY C. SWEANY, M.D., Medical Director of Research, Municipal Tuberculosis Sanitarium, Chicago, and Research Associate, Department of Physiology, University of Chicago. A volume of 265 pages with 73 illustrations. Published by Charles C. Thomas, Springfield, Illinois, 1941. Price: $5.00.

BOOK REVIEW

FRACTURES AND DISLOCATIONS. By EDWIN O. GECKELER, M.D., Orthopedist, Philadelphia, Pennsylvania. A volume of 307 pages with numerous illustrations. Published by The Williams & Wilkins Company, Baltimore, Maryland, 1940. Price: $4.00.

This book on fractures and dislocations for the practitioner is well indexed and illustrated and each chapter is followed by an adequate bibliography. The book is divided into two parts: the first concerning fractures, and the second dealing with dislocations. The present edition is the second, and as stated in the preface, emphasis is placed on fundamentals and simplicity of treatment. The text is easily read, with short, accurate descriptions of the injuries under discussion and the treatment to be employed. As is to be expected, the operative technic is not discussed, with the exception of such procedures as debridement, subcutaneous leverage, and skeletal traction, but the treatment in which manipulation and traction are employed is adequately described. It is rightly implied that surgical measures should be carried out by a surgeon especially trained in this type of work.

The general practitioner should be especially interested in the discussion on follow-up treatment, which is good throughout the text and has been well illustrated by simple exercises.

This work gives a detailed account, with illustrations, of the employment of skeletal traction. The question of the use of sulfanilamide in the treatment of compound fractures, a topic of much discussion in present-day literature, is only lightly touched upon, and the amount of the drug which is suggested for such cases is inadequate in view of the present understanding of its use.

This work is heartily recommended to the general practitioner for its clarity, concise information, and value as a reference book.

ABSTRACTS OF CURRENT LITERATURE

CONTENTS BY SUBJECT

THE FOLLOWING ABSTRACTORS HAVE CONTRIBUTED TO THIS ISSUE

W. R. Brooksher, M.D., of Fort Smith, Ark.
Q. B. Coray, M.D., of Salt Lake City, Utah
Percy J. Delano, M.D., of Chicago, Ill.
Sydney J. Hawley, M.D., of Danville, Penna.
Hans W. Hefke, M.D., of Milwaukee, Wis.
Lewis G. Jacobs, M.D., of Indianapolis, Ind.
John G. Menville, M.D., of New Orleans, La.
Lester W. Paul, M.D., of Madison, Wis.
Simon Pollack, M.D., of Tulsa, Okla.
Ernst A. Schmidt, M.D., of Denver, Colo.
Willis A. Ward, M.D., of Chicago, Ill.

ABSTRACTS IN THIS ISSUE LISTED ALPHABETICALLY BY AUTHORS

THE EAR

Carcinoma of the External Auditory Canal, Middle Ear, and Mastoid. Robert J. Bowman. Ann. Otol., Rhinol., and Laryngol., **49,** 225–231, March, 1940.

The subject of carcinoma of the external auditory canal, middle ear, and mastoid is reviewed. Most of the reported cases have been preceded by chronic infection. Pain is not an early symptom and by the time pain appears, the tumor will usually have been present for some time. In all cases of chronic otitis media, a possibility of the presence of carcinoma should be considered when the response to the ordinary course of treatment is at all unusual. Biopsies should be taken early and, if necessary, frequently in all cases in which suspicious granulations exist. The author reports three cases. The first was one of involvement of the external canal. Roentgen therapy was administered in fractional daily doses of 200 r up to a total of 3,650 r. Observation after a year and a half showed disappearance of the lesion and no evidence of recurrence. The second case was one of involvement of the mastoid in a patient who had had a chronically infected ear for 40 years. A combination of roentgen rays, surgery, and later radium was used in treatment but the patient died. The third patient had had bilateral chronically infected ears for 33 years. The diagnosis of carcinoma in the left ear was established after radical mastoidectomy failed to control the disease. Some improvement was noted after roentgen therapy but the disease was not controlled and death eventually ensued.

LESTER W. PAUL, M.D.

GAS GANGRENE

X-ray in Diagnosis and Treatment of Gas Gangrene. James F. Brailsford. British Med. Jour., **1,** 247–249, Feb. 17, 1940.

The author makes a plea for early roentgenograms in cases in which gas gangrene is suspected and for routine intensive treatment if the diagnosis is definitely made. It is stated that by roentgenography it is possible, within a few minutes and without any injury to the patient, to detect the formation of gas in the tissues before it has produced any clinical signs. Customarily, these cases are not x-rayed until the clinical signs are well advanced.

Regarding therapy, the author claims that, "up to this time no patient has died of gas gangrene who has received a treatment in the morning and a treatment in the evening for three days over all the involved tissues." The technic calls for 100 r per port, with the use of as many ports as necessary; voltage and filtration are recommended for ordinary cases. Surgery is indicated in many cases and should not be abandoned in favor of other forms of therapy. Reference is made to the occurrence of this condition in cattle.

Q. B. CORAY, M.D.

LUNGS, TRACHEA, AND BRONCHI

Curability of Primary Carcinoma of the Lung. Richard H. Overholt. Surg., Gynec., and Obst., **70,** 479–490, Feb. 15, 1940.

On the basis of an experience with 104 cases, Overholt is optimistic as to the operability rate in primary carcinoma of the lung, and believes that the cures should steadily rise. Prerequisites for its early discovery, all of which may be brought into play, are professional interest, a warning symptom which induces the patient to seek advice, the availability of chest roentgenograms, and histologic proof or denial of its presence. Surgical excision provides the only hope of cure and the time element is most important. There are but occasional rare exceptions to the general disappointing results from irradiation. Criteria of operability are discussed. Of the series, it was possible to obtain tissue for histologic verification in 72 per cent. A total of 21 per cent of the lesions was considered resectable. Of the verified cases, 11 per cent have lived following surgical resection for varying periods up to five years and ten months without evidence of recurrence.

W. R. BROOKSHER, M.D.

Tuberculous Ulcerogranuloma of the Trachea and Bronchi. Mervin C. Myerson. Ann. Otol., Rhinol., and Laryngol., **49,** 177–198, March, 1940.

Tuberculosis of the trachea and bronchi is of particular interest to the bronchoscopist. This aspect of the subject is considered in detail by the author. In a series of 52 ulcerogranulomatous lesions, the majority were found to be in the main and lobar bronchi. In three instances the lesion was in the trachea and one of the major bronchi, while in one only the trachea was involved. These granulomatous lesions may act in the same manner as foreign bodies and their effects are governed by the same laws. They may be partly obstructive, completely obstructive, or may obstruct only during expiration, causing a check-valve arrangement and a resulting obstructive emphysema.

LESTER W. PAUL, M.D.

Localized Emphysema as a Sign of Incomplete Bronchial Obstruction. James Maxwell. British Med. Jour., **1,** 520–522, March 30, 1940.

Of great interest to radiologists is the author's initial statement in this article to the effect that, in the first place, physical examination of the chest has recently tended to recede in importance, and second, it must be admitted that if the value of physical examination is compared to that of radiography in the average case of lung disease, the former yields decidedly less accurate information.

Types of bronchial obstruction are discussed under the headings of "pass valve," which causes only a wheeze: "stop valve," which prevents air from enter-

ing the section of lung involved, and "check valve," which causes progressive expansion of the lung below. Obstructive emphysema is caused by foreign body, tumor, or accumulated secretion. The heart may or may not be displaced. It may be necessary to make a roentgenogram in order to differentiate from spontaneous pneumothorax. The roentgen signs are discussed.

Six cases are reviewed which illustrate the subject under discussion. The author makes a plea for early and accurate diagnosis for the reason that such cases can thereby be treated much more effectively.

Q. B. Coray, M.D.

GASTRO-INTESTINAL TRACT

A Roentgenographic Study of the Normal Pylorus and Duodenal Cap. J. M. Painter, T. Wingate Todd, and Wilhelmine Kuenzel. Jour. Lab. and Clin. Med., **25**, 581–602, March, 1940.

In a roentgenographic study of the normal pylorus and duodenal cap, the authors made roentgenographic records of six specific substances and their controls. These substances were water, peppermint, soda, milk, buttermilk, and amyl nitrite. It was found that the gastroduodenal behavior patterns could be properly and interestingly analyzed by serial roentgenograms made at 10-second intervals.

The typical neutral pattern of the stomach was expressed in a peristalsis of both stomach and duodenum wherein the waves followed each other at 20-second intervals. The pylorus opened and closed every 20 seconds, and evacuation of gastric secretion recurred with every systole. A careful watch of the upper level of the fluid column in the stomach was found to be a good guide, as regards activity. This level fell if elimination exceeded secretion. If secretion exceeded elimination, the gastric shadow either elongated or widened. Water produced an increase of gastric secretion; both gastric and duodenal peristaltic waves were deepened. The neutral rhythm, however, was resumed in about 10 minutes. Peppermint had a similar but more forceful effect and maintained a patent pylorus. The pyloric rhythm was eliminated for a time only, but the rhythm of the gastric peristalsis, cap, and duodenum remained as in the neutral pattern. Soda produced an effect similar to that of peppermint, but the effect was not so transitory as that of water as it required from 15 to 20 minutes for return to the neutral pattern instead of only about ten minutes after the administration of water. Milk slowed down all rhythms and greatly weakened peristalsis in both the stomach and duodenum. It did not, however, hamper gastric elimination, but the retardation of rhythms resulted in mistiming. Buttermilk was found to slow down the rhythm of pylorus, as well as cap rhythm and evacuation, but was a powerful stimulant to gastroduodenal peristalsis and to gastric secretion. This caused a more thorough mixing of the barium sulphate. It did not modify the 20-second interval between successive waves, as was the case with milk. Amyl nitrite, in therapeutic doses, had a complete immediate inhibitory effect upon gastric peristalsis and fall of the fluid level. It did not, however, reduce gastric tone. It had slight but progressively less inhibitory effect upon pyloric rhythm, cap rhythm, evacuation rhythm, and duodenal peristalsis. The gastric response to the stimulus of a balloon was studied and found to be a marked increase in motility—the production of a great increase in the forcefulness of the waves. Six medical students served as subjects for the experiments.

Willis A. Ward, M.D.

Recent Advances in the Roentgen Diagnosis of Gastric Cancer. R. Ledoux-Lebard. British Jour. Radiol., **13**, 37–50, February, 1940.

The radiologist's object should be to promote the recognition of gastric cancer at the earliest possible moment. The diagnosis of early cancer is impossible by clinical means. Therefore, the roentgen examination should be made early. It should always be remembered that the classical symptoms of gastric cancer are those of advanced disease.

The belief that larger ulcers are necessarily cancer is misleading. The site of the niche is of greater importance in the differential diagnosis than its size. Ulcers on the vertical part of the lesser curvature rarely become malignant. Those on the horizontal part, between the incisura angularis and the pylorus, often are malignant. The more irregular the niche, the greater is the likelihood of cancer.

Every case in which there is doubt should be carefully followed. A progressively enlarging lesion is usually carcinoma.

In the very early case peristalsis may pass through the area of involvement, or may indirectly move the area of infiltration so that a deceptive appearance of normal peristalsis may be observed. Only by careful comparison of serial films is the lesion discovered. The most common early deformity of the outline is a "step-shaped" constant appearance.

The surgeon, by inspection and palpation, may not detect an early lesion which has been seen on the roentgenogram. Such patients should have a resection anyway. A few unnecessary operations may thus be performed, but the total bad results will not be as great as the danger of waiting in a case of cancer. When the cancer is large, it is usually too late for successful surgery.

Sydney J. Hawley, M.D.

The Importance of the Gastroscope in the Diagnosis of Gastric Diseases in the Army. Rudolf Schindler. British Med. Jour., **1**, 243–247, Feb. 17, 1940.

The author discusses very convincingly the situation of the recruit or ex-soldier who develops gastric symptoms which may or may not be due to organic changes in the stomach wall. Reference is made to the many

such examples which occurred in the German army during the last war. The importance of general examinations with special reference to roentgenography and fluoroscopy is pointed out. However, according to the author, it is quite obvious that many stomachs may be affected by inflammatory processes, generally known as gastritis, which cannot be demonstrated by x-ray examination. It is also stated, in passing, that the Schindler gastroscope is valueless in diagnosis of duodenal lesions. Thirteen cases were reviewed, in which various inflammatory processes were demonstrated and the patient treated accordingly. Symptoms of all these cases consisted of varying degrees of epigastric distress. Gastroscopy gave positive findings in ten of the thirteen cases and chronic gastritis was found to be the most frequent disease.

Q. B. CORAY, M.D.

Results of Ambulant Treatment of Peptic Ulcers. David Ferriman. British Med. Jour., **1,** 210–211, Feb. 10, 1940.

The author states that the data presented were obtained from cases which were, of necessity, treated outside of hospitals and that the results were such as to discredit the feeling for the necessity of hospitalization for cases of peptic ulcer. Comments are made on the pathology of the peptic ulcer and attention is called to the relation of nervous tension to the condition. It is pointed out, however, that the mere relief of nervous tension is insufficient and the usual alkaline and dietary régime must be followed.

The treatment outlined was a simple modified ulcer diet, and control was based on radiologic findings. The patient was admonished to continue treatment three months after cure was apparent from roentgenologic examination. The gastroscope was also used in checking results. The various faults of medical and surgical forms of treatment are discussed.

Q. B. CORAY, M.D.

Chronic Duodenal Stasis. Arthur Metz. Minnesota Med., **23,** 68–70, January, 1940.

The etiologic factor in duodenal stasis may be congenital or acquired. A congenital anomaly may cause pressure on the duodenum where it passes over the spine. The stasis may also be secondary to a mechanical obstruction, such as tumor or adhesions. The most common cause, in the author's experience, is pressure over the spine by the mesenteric attachment, usually associated with visceroptosis.

The symptoms vary from time to time and usually include nausea associated with loss of weight and weakness. In more severe cases there is vomiting associated with fullness in the upper right abdomen which comes on immediately after starting to eat. The patient sometimes ends the meal for fear of vomiting.

A positive diagnosis is made fluoroscopically. Sometimes slight delay is seen, sometimes there is dilatation, and, in severe cases, definite evidence of obstruction of the barium at some point.

Treatment is both medical and surgical. In cases in which obstruction is only slight, an attempt should be made to make the patient gain weight, so as to increase the amount of intra-abdominal fat and hence decrease the visceroptosis. In more advanced stages the patient should be kept in bed, with forced feedings. Sometimes lying on the left side, or face downward, will give relief. When the obstruction is of greater extent, relief must come from surgery.

PERCY J. DELANO, M.D.

Roentgen Ulcer of the Small Intestines. Fritz Meves. Röntgenpraxis, **12,** 48–53, February, 1940.

Radiation therapy to the upper abdomen after surgical removal of carcinoma of the stomach is not used routinely. The opinion of most surgeons and radiologists is that the results are not worth the effort. Complications of roentgen therapy in such cases might be early, as, for instance, x-ray dermatitis and damage to the parenchymatous organs of the abdomen, especially the intestines. Late post-radiation changes of the intestines are very difficult to diagnose and evaluate. The symptoms are vague and not characteristic.

A rare case of late post-radiation changes is reported. A 25-year-old male had radical surgery for the removal of a carcinoma of the stomach. About one week after the operation he received three times one erythema dose of x-ray during 12 days to an anterior abdominal field. He suffered from vomiting and nausea for two weeks afterward and his skin showed evidence of a marked x-ray dermatitis which required about six months to heal, with atrophy and telangiectases. There was no evidence of trouble for 15 years after the operation, at which time he complained of abdominal cramps and vomiting. Diarrhea was present at times. He was admitted to the hospital, with the diagnosis of incomplete small intestinal obstruction. Surgical exploration showed a stenotic area in the jejunum with dilatation proximal to it. The narrowed area was resected and showed histologic evidence of a chronic ulcer and vessel changes which were thought to be typical of late roentgen damage. Of interest were the absence of lymphatic nodes in the irradiated area and the presence of thick fibrous plaques over part of the small intestines.

The author believes that the rather excessive radiation therapy was responsible not only for the late damage to the small intestines, but probably also for a 15-year cure of a usually hopeless condition, namely, carcinoma of the stomach.

HANS W. HEFKE, M.D.

Inhibition Ileus. E. A. Heiberg. Minnesota Med., **23,** 94–96, February, 1940.

The term "inhibition ileus" is synonymous with paralytic ileus. The condition is seen most often in

cases of peritonitis. Penetrating abdominal wounds, the extravasation of blood, and mesenteric thrombosis are also etiologic factors. Paralytic ileus may also be of nervous origin, as the result of injuries and diseases of the spinal cord, or of fracture of the lower ribs, or of lead poisoning. It may be of toxic origin, as in pneumonia, uremia, undulant fever, meningitis, and empyema. It may be reflex, as noted in renal or gallbladder colic, torsion of an ovarian cyst, crushing of a testis, or strangulation of the spermatic cord.

A progressive dilatation of the bowel with a corresponding thinning of all the layers of the intestines is the only pathologic change noted in early paralytic ileus. Intestinal secretion is increased, while the venous stasis diminishes absorption from the bowel, so that large amounts of stagnant toxic fluid collect in the gut. The intra-abdominal exudate may be serous, fibrinous, or fibrino-plastic.

The pain is not intermittent, but dull and steady. As the tympanites increases, the pyloric sphincter relaxes, permitting abdominal contents to regurgitate into the stomach. Peristalsis is inhibited. X-ray examination may show a "ladder pattern" in the bowel.

Prophylaxis includes avoidance of surgical trauma, withholding of all post-operative liquids till vomiting has ceased, and the administration of morphine freely, since this drug increases the intestinal tonus.

Active treatment includes administration of fluids, saline, and glucose; Wangensteen recommends from $^1/_6$ to $^1/_3$ gm. per kilo body weight of chlorides. Prostigmin has given good results in the hands of some observers. Enterostomy may have to be resorted to, though the nasal suction method of Wangensteen has largely supplemented this, and probably drains the intestinal tract more thoroughly. Spinal anesthesia has been used by some surgeons as a treatment for paralytic ileus, since it causes inhibition of tonus in the sympathetic nerve fibers which send inhibitory impulses to the bowel, thus leaving it more fully under vagus control.

PERCY J. DELANO, M.D.

Intussusception: A Radiological Study. E. Rohan Williams. British Jour. Radiol., **13,** 51–70, February, 1940.

The roentgen examination of intussusception is a valuable diagnostic aid and occasionally a useful method of treatment. Texts and literature of roentgenology have neglected this subject.

Intussusception may be ileocecal, ileocolic, or colocolic. As the intussusception proceeds, the mesentery is compressed, giving rise to increasing edema, obstruction, and hemorrhage. It may occur in otherwise normal children, most often at the age of weaning. In adults it usually occurs as a result of a tumor. The symptoms are abdominal pain, palpable tumor, intestinal hemorrhage, and intestinal obstruction.

The roentgen signs are based on the anatomic situation, which is made up of three concentric cylinders. The contrast medium may flow between the outer and middle cylinders, producing a cupped effect, with complete arrest of the enema. It may flow through the inner cylinder, showing then a thin streak through the center of the obstruction. The enema may gradually move the obstruction proximally as it reduces the intussusception.

A large fecal mass or a pedunculated tumor may present the same appearance. A large quantity of gas in the cecum may prevent homogeneous filling and give an appearance similar to intussusception.

Barium by mouth should be used only when a chronic intussusception is suspected. The appearance produced with peroral barium is dilatation of the bowel proximal to the obstruction and a gradual narrowing, which corresponds to the intussusception; occasionally, the sheaths may be visualized.

A plain film should always be made. This will often indicate the approximate location of the lesion and will sometimes identify it.

Attempts to reduce the intussusception by the enema should not be made in the presence of toxemia or peritonitis, and in any case should be done under fluoroscopic control.

SYDNEY J. HAWLEY, M.D.

THE HEART

Traumatic Constrictive Pericarditis. E. E. Glenn. Jour. Missouri Med. Assn., **37,** 7–11, January, 1940.

The author reports a case of chronic constrictive pericarditis which followed a crushing injury to the chest. While the etiology of this condition often is difficult to determine, trauma as a cause has not been mentioned with any frequency. The author's patient developed signs and symptoms of cardiac disease about two years after a severe injury to the chest. Roentgen examination revealed no enlargement of the heart but cardiac movements were limited. Roentgen kymography showed an area of decreased amplitude of movements of the left ventricle, more suggestive of infarction than pericarditis. Because of rapid recurrence of ascites, operation was done, since a positive diagnosis could not be made and it was felt that an omentoplexy might give some relief. The patient died and autopsy revealed pericardial constriction by dense adhesions. The author emphasizes the difficulty in arriving at a correct diagnosis even though Beck's diagnostic triad be present.

LESTER W. PAUL, M.D.

THE KIDNEY

Spontaneous Gas Pyelogram. Olle Olsson. Acta Radiol., **20,** 578–584, December, 1939.

In an elderly diabetic woman the spontaneous gas filling of the renal pelvis and calices and of parenchymal cavities allowed the x-ray diagnosis of pyelonephritis and papillary necrosis. The etiologic factor was apparently *B. coli.* The gas formation was due to sugar

fermentation in the urine. Later autopsy findings confirmed the roentgenologic diagnosis in every detail.

ERNST A. SCHMIDT, M.D.

Solitary Pelvic Ectopic Kidney. Nelse F. Ockerblad and Hjalmar E. Carlson. British Jour. Urol., 12, 43–48, March, 1940.

The authors present a case of solitary pelvic ectopic right kidney in a female, 36 years of age. The diagnosis was made six years previous to the patient's death, which resulted from nephritis. Autopsy showed a congenital absence of the kidney, fallopian tube, and ovary.

JOHN G. MENVILLE, M.D.

THE PINEAL BODY

Pineal Localization: A Rapid Direct Method. E. Peter Allen. British Jour. Radiol., **13,** 102–104, March, 1940.

The construction of charts made of a transparent base, such as unexposed x-ray film, following the Vastine-Kinney method, is described. The charts are placed over the film and the pineal localization is thus more quickly obtained than with the original method.

SYDNEY J. HAWLEY, M.D.

PROTECTIVE MEASURES

Protection in Radium Teletherapy at Westminster Hospital: A Summary of Measurements of Gamma-ray Doses Made over a Number of Years with Condenser Ionization Chambers Carried by the Staff. C. W. Wilson. British Jour. Radiol., **13,** 105–107, March, 1940.

Members of the staff carried condenser ionization chambers during a period of observation from November, 1933, to April, 1939. Results showed that operators never received more than 0.25 r per day.

SYDNEY J. HAWLEY, M.D.

THE SKULL

Turricephaly, Turmschädel, or Oxycephaly, with Craniostenosis. S. J. Webster and J. E. Morgan. Ohio State Med. Jour., **36,** 277–280, February, 1940.

The authors report a case of oxycephaly in a white male, aged 22. The films show the typical increased digital impressions, closed suture lines (premature synostosis), and increase in the relative vertex-base diameter of the skull. The skull deformity had been noted since infancy and was probably due to a congenital dysgenic malformation of the skull bones. The only associated findings were a contraction of the visual fields and secondary optic atrophy.

SIMON POLLACK, M.D.

SYPHILIS

The Roentgen Therapy of Progressive Paralysis. F. Bering. München. med. Wchnschr., **87,** 229–230, March 1, 1940.

In 15 cases of syphilis of the brain (general paralysis of the insane) in which malarial therapy was contraindicated, roentgen irradiation was administered to the head. A dose of 440 r (H.V.L. $_{Cu}$ = 1 mm.) divided into four treatments was given. This produced a marked reduction in the cerebrospinal fluid lymphocytosis and a striking amelioration of symptoms; for instance, in one of the cases epitomized the patient was restored to ability to do semi-skilled work as a mechanic, from an advanced stage of the disease with hallucinations. One patient died of edema of the brain; temporary epilation occurred in all cases. No other serious ill effect was observed. On account of this one death, it was thought advisable in future cases to increase the time between the treatments (the spacing is not stated, however). The author believes the method should be used whenever malarial therapy is contraindicated.

LEWIS G. JACOBS, M.D.

THE THYROID GLAND

Inflammatory Disease of the Thyroid Gland. Thomas O. Young. Minnesota Med., **23,** 105–111, February, 1940.

The inflammatory lesions of the thyroid gland are characterized by lymphocytic invasion and connective tissue proliferation; they are broadly classifiable into a group in which the infective agent is specific, and a group in which it is not.

The specific infections include tuberculosis, syphilis, actinomycosis, and echinococcus disease.

The non-specific infections include acute thyroiditis, with or without abscess formation, Riedel's struma, Hashimoto's struma, strumitis, and lymphocytosis, and fibrosis (slight to moderate).

Acute thyroiditis without abscess formation frequently follows acute infections elsewhere in the body, such as abscessed teeth, tonsillitis, and upper respiratory infections. Abscess formation may be productive of the gravest results, and calls for prompt surgical intervention.

Chronic thyroiditis may be associated with hypothyroidism.

In Riedel's struma, the gland is very hard, indurated, and fixed. A diagnosis of cancer is made in 90 per cent of the cases. Dysphagia, dysphonia, swelling, and tenderness, with occasional symptoms of mild hyperthyroidism, may be present.

In 1912 Hashimoto reported four cases of diffuse lymphocytic infiltration of the thyroid. In contrast to Riedel's struma, there is no involvement of adjacent structures, adding to the technical difficulty of operation.

In 12 cases of chronic thyroiditis, eight were females,

four males, with an average age of 49. Average duration of symptoms was 195 days. Thyroidectomy was performed in eight cases, x-ray therapy was used in two, and two cases were treated medically.

In seven cases of acute thyroiditis, six were females and one a male, with an average age of 46. Average duration of symptoms was 35 days.

In all, 26 cases of inflammatory disease occurred in a series of 2,900 thyroidectomies. Results in those treated surgically were good.

PERCY J. DELANO, M.D.

TUBERCULOSIS

Tuberculosis: Its Two Clinically Demonstrable Phases of Evolution. C. A. Stuart. South. Med. and Surg., **102,** 1–4, January, 1940.

The evolution of tuberculosis passes through two broad, clinically demonstrable phases of development. The phenomena that produce the clinical picture of the first phase of the disease (primary tuberculosis) include the transient initial (pre-allergic) fever, the entry of tubercle bacilli into the gastro-intestinal tract, the acquisition of sensitiveness to tuberculoprotein, the development of primary tuberculous lesions, and the gradual resolution of these lesions which converts them into fibroid or calcified deposits. Clinical studies have demonstrated that tubercle bacilli may be recovered from the gastric contents several days before cutaneous sensitivity to tuberculin makes its appearance. The interval between the initial entry of tubercle bacilli into the body and the acquisition of sensitiveness to tuberculoprotein varies from three to eight or more weeks. During this pre-allergic period, tubercle bacilli may be widely disseminated to various regions of the body. Evidence has accumulated which suggests the desirability of revising the present view, which tends to limit the primary tuberculous complex to the focus of primary implantation and its secondary metastatic lesions in adjacent lymph nodes. The tendency for gradual slow resolution of these primary lesions is characteristic for this phase of tuberculosis regardless of the location of the lesions, whether in the thorax or elsewhere. The second demonstrable phase of tuberculosis is exemplified by such distinct clinical conditions as chronic pulmonary tuberculosis, osteoarticular tuberculosis, etc. (reinfection tuberculosis). This phase materializes in only a minority of infected tuberculin-sensitive patients. Occasionally the interval separating the two phases of the disease is so short that complete involution seems to be a single, continuous process. Some tuberculin-sensitive patients presenting no evidence of clinical tuberculosis during post-infection periods of considerable length eventually acquire tuberculosis of various extrathoracic organs or tissues and this is interpreted as conclusive evidence that these clinical forms of the disease are special examples of tuberculosis in its second or reinfection phase of development. This phase of the disease is characterized clinically by its tendency to cause progressive tissue destruction, to produce symptoms of gradually increasing severity requiring active therapy, and to cause illness and death.

LESTER W. PAUL, M.D.

THE UTERUS

Carcinoma of the Cervix Uteri: Factors Influencing Prognosis. Harry H. Bowing. Minnesota Med., **23,** 85–93, February, 1940.

Bowing enumerates the following factors as being of importance in the prognosis of carcinoma of the cervix uteri: (1) extent of the local lesion; (2) age of the patient; (3) general health and vigor; (4) resistance to the malignant growth.

The extent of the local lesions is usually described in stages. Stage 1 denotes that the primary lesion is limited to the cervix; Stage 2 includes, also, moderate infiltration of the vaginal wall or the parametrial tissues; in this stage the uterus is movable. In Stage 3 there is sufficient parametrial invasion to result in definite fixation of the uterus, and in Stage 4 the pelvic structures are extensively invaded and fixed.

Cancer appears to have a more grave prognosis in younger individuals. Biopsy is considered to carry little or no risk.

More than 90 per cent of malignant lesions of the cervix are squamous-cell epithelioma, from about 5 to 8 per cent are adenocarcinoma, and the remainder are a combination of the two.

The radium technic employed in the author's clinic may be defined as an intensive multiple or broken-dose method. The radium or radon content of the universal tubes is in the range of 50 mg., or millicuries, respectively. The filters are kept constant. Radium is supplemented with deep roentgen therapy. In the period from 1915 to 1929, there were 29.1 per cent of five-year cures; this covered 1,491 cases treated, of which 1,245 were subsequently traced.

PERCY J. DELANO, M.D.

Transvaginal X-ray Treatment of Cervical Cancer. Arthur W. Erskine. Wisconsin Med. Jour., **39,** 184–187, March, 1940.

A method for the transvaginal x-ray treatment of cervical cancer is described. A multiple blade, expanding speculum is used, and, after insertion into the vaginal canal, it is fully expanded and attached to the tube stand. With this apparatus the focus–surface distance is 28 cm. Isodose charts are reproduced, showing the distribution of radiation with several openings of the speculum. The author gives three doses of 1,170 r each, measured in air, at weekly intervals at the start of the series of cross-fire treatments through external parts and three similar doses at the end of the cross-fire series. A single dose of 1,170 r is given after one month's rest and repeated one month later. Erskine is convinced that the results are better than when radium is used.

LESTER W. PAUL, M.D.